Neuropsychological and socio-emotional processing in children and adolescents with Anorexia Nervosa

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ABSTRACT

Anorexia Nervosa (AN) is an eating disorder associated with high morbidity rates and considerable functional and psychosocial impairment. Effective treatments for AN are lacking, and therefore research approaches geared towards understanding possible underlying mechanisms are desirable, as they may provide new targets for treatments.

The overall aim of this thesis was to investigate neuropsychological and socio-emotional processing in children and adolescents with AN, and improve knowledge of how such characteristics may be important in the pathogenesis and maintenance of AN.

Specifically, studies 1 and 2 aimed to investigate cognitive processing (specifically set shifting and central coherence) in children and adolescents with AN and unaffected mothers of offspring with AN. Study 3 aimed to investigate the feasibility and acceptability of self-help Cognitive Remediation Therapy (CRT) delivered in a family context. Studies 4 and 5 both aimed to investigate socio-emotion processing (specifically, emotion recognition and emotion expression) in AN across a large age range.

The results from study 1 showed that children and adolescents with AN possessed an inefficient cognitive processing style characterised by higher levels of perseveration and less holistic processing. Study 2 revealed that unaffected mothers of offspring with AN also demonstrated an inefficient cognitive processing style in comparison to healthy control mothers of healthy control offspring. Study 3 provided preliminary data to suggest that self-help CRT is an acceptable form of treatment for AN. Study 4 demonstrated subtle but specific difficulties in the recognition of sadness in individuals with AN. This ability was more problematic in younger individuals with AN. Lastly, study 5 demonstrated altered positive emotion expressivity in individuals with AN, with lower levels of emotion expressivity being associated with a more clinically severe sub-group of participants.

These findings have implications for our understanding of the role cognitive and socio-emotional processing styles may play as important aetiological and

maintaining factors in AN. Furthermore, they also carry important clinical implications for AN, firstly by indicating that remedial treatments may be beneficial for both children and adolescents and family members. Secondly, they also provide direct targets for treatments aimed at improving social-emotional functioning.

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LIST OF ABBREVIATIONS

AN	Anorexia Nervosa
APA	American Psychiatric Association
APD	Avoidant Personality Disorder
AQ	Autism Quotient
ASD	Autism Spectrum Disorder
BED	Binge Eating Disorder
BOLD	Blood-Oxygen-Level Dependent
BMI	Body Mass Index
BN	Bulimia Nervosa
BPD	Borderline Personality Disorder
CAT	Cognitive Analytic Therapy
CBT	Cognitive Behaviour Therapy
CBT-AN	Cognitive Behaviour Therapy for Anorexia Nervosa
CBT-E	Cognitive Behaviour Therapy for Eating Disorders
CCI	Central Coherence Index
CDC	Centers for Disease Control & Prevention
CHOCI	Children's Obsessive Compulsive Inventory
CI	Confidence Interval
CREST	Cognitive Remediation and Emotion Skill Therapy
CRT	Cognitive Remediation Therapy
DFLEX	Detail and Flexibility Questionnaire
dMPFC	dorso-Medial Prefrontal Cortex
DSM-5	Diagnostic and Statistical Manual of Mental Disorder, 5th edition
DSM-IV	Diagnostic and Statistical Manual of Mental Disorder, 4th edition
EABT	Emotional Acceptance Behavior Therapy
ED(s)	Eating Disorder(s)
EDEQ	Eating Disorder Examination Questionnaire
EDNOS	Eating Disorder Not Otherwise Specified
FACS	Facial Activation Coding System
FACES	Facial Expression Coding System
FBT	Family Based Treatment
fMRI	functional Magnetic Resonance Imaging
FPT	Fragmented Pictures Task
FSIQ	Full Scale Intelligence Quotient
GEFT	Group Embedded Figures Test
GWAS	Genome Wide Association Study
HADS	Hospital Anxiety and Depression Scale
HC	Healthy Control
HPA	Hypothalamic Pituitary-Adrenal
IBW	Ideal Body Weight
IDEDST	Intra Dimensional Extra Dimensional Shift Task
IPT	Inter Personal Therapy
IQ	Intelligence Quotient
IQR	Inter Quartile Range
MANTRA	Maudsley Model of Anorexia Nervosa Treatment for Adults
NART	National Adult Reading Test

NHS	National Health Service
NICE	National Institute of Clinical Excellence
OA	Object Assembly
OCD	Obsessive Compulsive Disorder
OCI	Obsessive Compulsive Inventory
OCPD	Obsessive Compulsive Personality
OCPT	Obsessive Compulsive Personality Traits
OSFED	Other Specified Feeding or Eating Disorders
OFT	Overlapping Figures Test
OI	Order Index
PANAS	Positive and Negative Affect Scale
PET	Positron Emission Tomography
PIQ	Performance Intelligence Quotient
PLW	Pointlight Walkers
PRISMA	Preferred Reporting Items for Systematic Reviews & Meta-analysis
rCBF	regional Cerebral Blood Flow
RCT	Randomised Controlled Trial
ROCFT	Rey Osterrieth Complex Figure Test
RO-DBT	Radically Open-Dialectical Behavior Therapy
SAS	Social Anhedonia Scale
SCID	The Structured Clinical Interview for DSM-IV
SD	Standard Deviation
SE	Standard Error
SI	Style Index
SPECT	Single Photon Emission Computed Tomography
SS	Set shifting
SSCM	Specialist Supportive Clinical Management
TMT	Trail Making Task
ToM	Theory of Mind
VIQ	Verbal Intelligence Quotient
WASAS	Work and Social Adjustment Scale
WASI	Wechsler Abbreviated Scale of Intelligence
WCC	Weak Central Coherence
WCST	Wisconsin Card Sorting Test
WHO	World Health Organisation

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STATEMENT OF WORK

Chapter 1

The candidate completed thorough searches of the literature independently. For the published systematic reviews and meta-analyses, searches were conducted by the candidate and checked by co-authors and the first supervisor, Dr Kate Tchanturia. Dr Daniel Stahl (statistician), provided statistical consultations and advice for these publications. The interpretations were made by the candidate in conjunction with Dr Kate Tchanturia and the other co-authors.

Chapters 3, 4, 6 and 7

The candidate recruited the participants for these studies. The Child and Adolescent Eating Disorder Service, Adult inpatient and outpatient services at South London & Maudsley NHS Trust and the Vincent Square Eating Service helped with the recruitment of participants with Anorexia Nervosa. The candidate collected the data with the help of Samantha Lloyd. The candidate performed the initial data analyses, and Dr Mizanur Khondoker (statistician), provided statistical consultations and advice for these publications. The interpretations of this data were the result of the candidate's own work in in conjunction with Dr Kate Tchanturia (first supervisor) and the co-authors of the various manuscripts.

In addition to this, Marcela Marin Dapelo (PhD student, first supervisor: Dr Kate Tchanturia) contributed half of the dataset for study 4 (chapter 6). The candidate has joint first authorship of this manuscript with Marcela Marin Dapelo.

Chapter 5

The candidate amended the Cognitive Remediation Therapy manual with the help of Dr Kate Tchanturia. The training and focus groups for this study were co-facilitated by the candidate and Dr Kate Tchanturia. The candidate transcribed and analysed the interview transcripts. The interpretations of this data were the result of the candidate's own work in in conjunction with Dr Kate Tchanturia and the co-authors of the various manuscripts.

PUBLICATION LIST

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Tchanturia, K., & **Lang, K.** (2014).Cognitive Profiles in adults and children with Anorexia Nervosa and how they have informed us in developing CRT for Anorexia Nervosa. Chapter in *Cognitive Remediation Therapy (CRT) for Eating and Weight Disorders*. Eds Tchanturia, K.

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OTHER DISSEMINATIONS

Oral presentations

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STRUCTURE OF THIS THESIS

This thesis incorporates publications, an alternative route for PhD submissions.

Chapter 1 provides an overview of Anorexia Nervosa (AN) and neuropsychological processing and socio-emotional processing within AN. Three published reviews of the literature are included within this chapter.

Chapter 2 provides details of the general methods used for each study.

Chapters 3, 5 and 6 correspond to published papers.

Chapter 4 is an empirical study that has been accepted for publication with minor amendments and is not yet available. Therefore the most recent version of the manuscript is included here in a chapter format.

Chapter 7 is an empirical study that is currently under-review in a peer-reviewed journal. The most recent version of the manuscript is included here, in chapter format.

Lastly, chapter 8 provides a general discussion of the key findings, strengths and limitations and concluding remarks.

Figure 1 provides a map of the structure of the thesis.

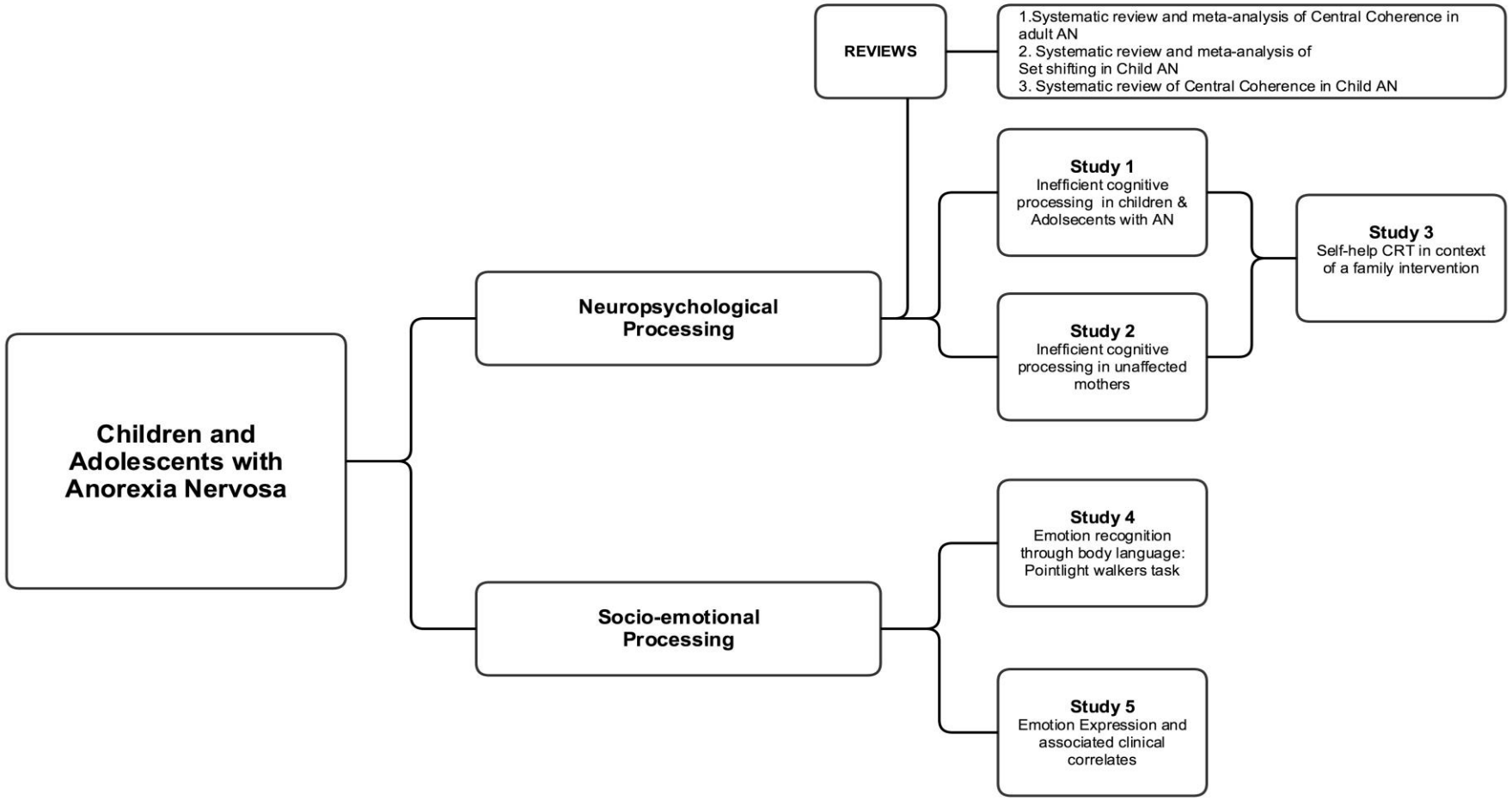

Figure 1: Map of thesis

CHAPTER 1:

INTRODUCTION

1.1 FEEDING AND EATING DISORDERS

Eating disorders (ED) are serious psychiatric illnesses characterised by abnormal or disturbed eating or eating related behaviours that significantly impair physical health or psychosocial functioning (American Psychiatric Association, 2013).

The introduction of the fifth edition of the Diagnostic and Statistical Manual (DSM-5) now includes a revised chapter entitled 'Feeding and Eating Disorders'. Feeding and eating disorders encompass seven disorders including the long standing categories of both Anorexia Nervosa (AN) and Bulimia Nervosa (BN), as well as the newly added diagnosis of Binge Eating Disorder (BED) and the newly named Other Specified Feeding or Eating Disorders (OSFED), which had formerly been known as Eating Disorders not otherwise Specified (EDNOS) (Table 1).

Disorder	Characteristics
Pica	Persistent eating of non-nutritive or non-food substances over a period of a month or more.
Rumination disorders	Repeated regurgitation of food after eating, in the absence of nausea, involuntary retching, or disgust.
Avoidant/Restrictive Food Intake Disorder	Previously named 'feeding disorders of infancy or early childhood' in DSM-IV. Characterised by avoidance/restriction of food intake with failure to meet nutritional requirements.
Anorexia Nervosa	Intense fear of fatness leading to restriction of energy intake, leading to significantly low body weight.
Bulimia Nervosa	Recurrent episodes of binge eating and inappropriate compensatory behaviours to prevent weight gain. Also characterised by negative self-evaluation in the context of weight and shape.
Binge Eating Disorder	Recurrent episodes of binge eating occurring on average at least once per week, over a period of three months.
Other Specified Feeding and Eating Disorders	Symptoms characteristic of an eating or feeding disorder, causing clinically significant distress or impairment but not meeting the full criteria of any disorder.

Table 1: Brief description and characteristics of the feeding and eating disorders in DSM-5.

1.2 ANOREXIA NERVOSA

At the start of this thesis the Diagnostic and Statistical Manual IV criteria for AN was in use (DSM-IV (American Psychiatric Association, 2000)), however, as of 2013 the fifth edition of the DSM was introduced, with changes to the diagnostic criteria for AN. The current criteria for AN are presented in table 2.

A.	Restriction of energy intake relative to requirements, leading to significantly low body weight in the context of age, sex, developmental trajectory, and physical health.
B.	Intense fear of gaining weight or of becoming fat, or persistent behaviour that interferes with weight gain, even though at significantly low weight.
C.	Disturbance in the way in which one views one's body or weight or shape on self-evaluation, or persistent lack of recognition of seriousness of the current low body weight.

Table 2: DSM-5 diagnostic criteria for AN.

AN is characterised by the core features of maintenance of low weight due to an intense fear of fatness and a disturbance in body perception. Low weight can be maintained through calorie restriction or other behaviours, such as excessive exercise or laxative misuse.

There have been several key changes to the diagnostic criteria of AN in DSM-5.
Firstly, DSM-5 has clarified the language used to describe the weight loss criterion (Criterion A). Criterion A has been amended so that individuals no longer need to articulate a refusal to gain or maintain a healthy weight, and now clinicians can use behavioural evidence to fulfil this criterion. Clarifications have also been made in regards to the definition of weight loss. The wording of DSM-IV had implied that a weight of less than 85% of what would be expected for an individual's height and age qualified as underweight. The modified criterion of DSM-5 acknowledges individual differences in the definition of 'healthy' weight, and has removed a

definitive marker of underweight status. It suggests that a combination of published thresholds (Centers for Disease Control & Prevention, CDC; World health Organisation, WHO), and clinical judgment based on clinical and physiological information should be used to guide this decision.

In adults a body mass index (BMI, kg/m^2) of 18.5 or lower has been classified as being underweight (Centers for Disease Control & Prevention, 2002) whereas a BMI of 17.0 or under is considered to be significantly underweight. In children, BMI percentiles (BMI-for-age) or percentage ideal body weight (%IBW) are used to estimate weight, taking into consideration developmental trajectories. A BMI-for-age below the 5th percentile or 15% lower than the IBW is considered underweight, with some research studies classifying 95% IBW as in remission (Lock et al., 2010).

Another key difference to be noted in DSM-5 is the removal of the amenorrhea criterion (Criterion D), to take into account the lack of this symptom in males, pre-pubertal females and also females using contraceptives.

The expansion of the low weight threshold and the deletion of Criterion D are expected to decrease the reliance on the OSFED diagnostic category in DMS-5 (formally known as EDNOS and the largest diagnostic category in DSM-4). It is anticipated that these minor changes will have a significant impact on the prevalence rates of AN, by reassigning patients who would not have meet the full diagnostic threshold for AN under DSM-IV criteria (Mancuso et al., 2015).

In summary, the modifications to the diagnostic criteria of AN in DSM-5 have increased the reliance on clinical judgement in the diagnosis of AN. Furthermore, such changes aim to reduce the preponderance of patients diagnosed with OSFED, whilst maintaining the clinical validity of the AN diagnosis (Brown, Holland, & Keel, 2014).

1.3 ONSET, EPIDEMIOLOGY AND CLINICAL COURSE

The onset of AN typically occurs during adolescence, with an increased risk for females (American Psychiatric Association, 2013; Hoek & Van Hoeken, 2003). Females aged between 15 and 19 years of age are considered a particularly high-risk group (Hoek, 2006; Smink, Van Hoeken, & Hoek, 2012), although diagnoses of pre-pubertal AN appear to be increasing (Nicholls, Lynn, & Viner, 2011). A recent review by Smink et al. (2012) described the incidence rates of AN to be between 490 and 1204 per 100,000 person-years for community studies, and a more conservative estimate of 4.2 to 7.7 per 100,000 person-years ascertained from general practitioner records. Whether or not the incidence of AN has been steadily increasing over the last decade has been debated. A Danish population study examining time trends in incident rates suggested that although there had been a rise in the incidence of AN diagnoses, the increase was most likely attributable to a general increase in the diagnosis of all psychiatric conditions (Steinhausen & Jensen, 2015). The lifetime prevalence of AN is estimated to be between 2.4 and 4.2% (Bulik et al., 2006; Keski-Rahkonen et al., 2007; Wade, Bergin, Tiggemann, Bulik, & Fairburn, 2006).

In adults, AN typically has a prolonged and chronic course, with a significant number of patients continuing to experience clinically relevant symptoms following treatment intervention. Steinhausen (2009) reviewed the outcomes of AN patients in 199 studies and found that 46% showed full recovery at follow-up, 34% showed partial recovery and the remaining 20% remained chronically ill. Psychosocial outcomes following treatment are also poor for adults with AN, with a large proportion of patients reporting significant social impairment due to eating disorder related symptoms (Zipfel, Löwe, Reas, Deter, & Herzog, 2000).

For children and adolescents there is a slightly brighter picture with regard to course and outcome. Early intervention in AN is highly recommended as studies have demonstrated that treatment within three years of diagnosis predicts a more favourable prognostic outcome (Treasure & Russell, 2011). A majority of long-term follow-up studies have demonstrated recovery rates of between 67 and 76% at 10-

year follow-up (Herpertz-Dahlmann et al., 2001; Nilsson, Gillberg, Gillberg, & Raastam, 1999; Strober, Freeman, & Morrell, 1997; Wentz, Gillberg, Anckarsäter, Gillberg, & Råstam, 2009). Nevertheless, AN still follows a protracted course in adolescents, (Herpertz-Dahlmann et al., 2001). There are also significant psychosocial improvements following treatment in younger patients with an earlier onset. Herpertz-Dahlmann et al. (2001) found no differences between recovered AN patients and matched healthy controls (HCs) in psychosocial outcome variables such as number of social contacts or dependency on family members.

AN has one of the highest mortality rates amongst psychiatric disorders (Arcelus, Mitchell, Wales, & Nielsen, 2011; Hoek, 2006). Mortality rates are lower in child and adolescent populations than in adults and patients with a later illness onset (Arcelus et al., 2011). A recent meta-analysis highlighted that older age at first presentation was a strong predictor of mortality; whereas presentation at a younger age was associated with better outcome (Arcelus et al., 2011).

1.4 TREATMENT

1.4.1 Psychological therapies

At present the National Institute of Clinical Excellence (NICE) has no 'gold standard' recommended first-line treatment for adults with AN, although psychological therapy is the treatment of choice. The guidelines recommend that outpatient treatment should be offered in the first instance, with specialised multi-disciplinary inpatient care for more severe cases (NICE, 2004).

For adults there is 'grade C' level evidence (evidence gathered from expert opinion and not the result of randomised controlled trials (RCTs)) for the use of Cognitive Behavioural Therapy (CBT), Cognitive Analytic Therapy (CAT) and Interpersonal Therapy (IPT). Results of recent systematic reviews and meta-analyses have continued to support these guidelines, as although they suggest a slight improvement in treatment outcomes (particularly in support of CBT), they do not indicate a clear front-runner in the treatment for AN (Hay, 2013; Watson & Bulik, 2013).

A range of psychological therapies have been modified and developed to specifically treat AN (Hay, Claudino, Touyz, & Abd, 2015). These treatments aim to address the core psychopathology of the disorder, as well as often offering nutritional support and care (Hay et al., 2015). For example, Cognitive Behaviour Therapy for Eating Disorders (CBT-E) contains a number of modules aimed at addressing both eating and weight issues and the vulnerability and maintaining factors of AN, such as mood, relationships, perfectionism and self-esteem. CBT-E also places a direct emphasis on an increased calorie diet, aiming to maintain a BMI of 19 or above (Murphy, Straebler, Cooper, & Fairburn, 2010).

Results from RCTs for CBT-E are promising in regards to weight-restoration; however, further research to improve treatment outcomes for adults with AN is needed (Byrne, Fursland, Allen, & Watson, 2011).

Patients with severe and enduring AN have posed a further challenge to health services, and treatments have been tailored to meet the complex needs of this sub-group of patients (e.g. CBT for AN (CBT-AN, (Touyz et al., 2013)) or Specialist Supportive Clinical Management (SSCM, (McIntosh et al., 2005)). These treatments place less emphasis on nutritional recovery and weight status and more emphasis on achievable functional gains that could positively impact quality of life (McIntosh et al., 2006; Touyz et al., 2013).

The NICE guidelines recommend family-based treatments (FBT) for children and adolescents with AN (NICE, 2004). Treatment should aim to include a range of family members such as parents and siblings. To date there have been six published randomised controlled trials assessing the efficacy of FBT (Eisler et al., 2000; Le Grange, 1999; Lock, Agras, Bryson, & Kraemer, 2005; Lock et al., 2010; Robin et al., 1999; Russell, Szmukler, Dare, & Eisler, 1987).

Russell et al. (1987) provided the first evaluation of FBT, demonstrating its superiority over a non-specialised individual therapy on weight gain and measures of psychosocial functioning in individuals with early onset AN. This superiority was maintained over a 12 month follow-up period. Le Grange, Eisler, Dare, and Russell (1992) assessed two forms of FBT for AN, finding that both were effective in restoring weight and improving psychological outcomes, such as attitudes towards eating. More recently Lock et al. (2010) compared FBT to adolescent-focussed individual therapy. There were considerable improvements in weight gain across both groups; however, FBT was superior over all long-term follow-up points. Despite these positive outcomes regarding FBT with adolescents, there is still a significant proportion of non-responders to this treatment (Agras et al., 2004).

EDs are extremely costly disorders with an estimated cost of £70 million to the National Health Service (NHS), and approximately £1.25 billion to the UK economy (also accounting for loss of earnings of carers) per annum (BEAT, 2012). There is therefore a drive for the development of cost-effective treatments that also consider the involvement and wellbeing of carers and family members (Goddard, Raenker, & Treasure, 2012).

1.4.2 Psychopharmacology

Pharmacological treatments for AN show poor clinical efficacy, as well as high attrition rates (Hay & Claudino, 2012; Kishi, Kafantaris, Sunday, Sheridan, & Correll, 2012). Medications are often poorly adhered to, and the biological effects are often reduced due to the nutritionally compromised state of patients. The most recent guidelines suggest that there is weak to moderate evidence for the administration of zinc supplements and atypical antipsychotics in AN (Aigner, Treasure, Kaye, & Kasper, 2011).

1.5 COMORBIDITY

AN is associated with significantly high levels of psychiatric comorbidity, which are likely to complicate treatment and contribute to its poor prognosis.

1.5.1 Obsessive Compulsive Disorder (OCD)

AN and OCD frequently co-occur, with lifetime prevalence rates of OCD estimated to be between 9.5 and 62% in individuals with AN (Godart, Flament, Perdereau, & Jeammet, 2002; Kaye et al., 2004). There is also evidence to suggest that OCD precedes the onset of AN in many cases (Kaye et al., 2004; Swinbourne et al., 2012; Swinbourne & Touyz, 2007). A recent population-based study including 19,814 individuals with OCD and 8,462 individuals with AN, as well as matched HCs found females with OCD carried a 16-fold increased risk of developing AN (Cederlöf et al., in press). There is a significant overlap in symptomatology between AN and OCD and evidence of common aetiology between the two disorders, such as a similar genetic vulnerability (Cederlöf et al., in press) and dysregulation of the serotonergic system (Kaye, Wierenga, Bailer, Simmons, & Bischoff-Grethe, 2013; Maia & Cano-Colino, 2015). A longitudinal study by Micali et al. (2011) demonstrated that childhood OCD was a risk factor for the development of ED symptomology, as 12.7% of participants had a clinical diagnosis of an ED at follow-up.

1.5.2 Anxiety disorders

There are a number of studies suggesting that a majority individuals with AN also have a diagnosis of one or more comorbid anxiety disorders (Godart et al., 2002; Kaye et al., 2004). In the largest study to date assessing the comorbidity of AN and anxiety disorders, 53% of individuals with a diagnosis of AN also had a diagnosis of one or more comorbid anxiety disorders. These included social phobia (21%), specific phobia (14%), generalized anxiety disorder (13%), panic disorder (9%), post-traumatic stress disorder (5%) and agoraphobia (3%) (Kaye et al., 2004).

1.5.3 Mood disorders

Depression is a core feature of AN, and difficulties with mood regulation are a central element of many causal and maintenance models of the disorder. Several studies have demonstrated high rates of comorbidity between AN and depression (Lewinsohn, Striegel-Moore, & Seeley, 2000; Santos, Richards, & Bleckley, 2007; Zaider, Johnson, & Cockell, 2000), with estimates ranging from 31% to 88.9%. However, a number of these studies have not employed HC groups in their design, and as mood disorders are known to be common in the general population (estimates of up to 20%, (Kessler, Sharp, & Lewis, 2005)), it is difficult to estimate the true prevalence rate of mood disorders in AN populations.

Godart et al. (2015) recently addressed this methodological shortcoming by investigating the lifetime prevalence of mood disorders in AN and matched HCs, finding significantly higher rates of mood disorders (major depression, bipolar disorder and dysthymic disorder) in AN compared to HC. Specifically, they found comorbidity rates of 76.4% and 85.5% for AN-restrictor and AN-binge/purge subtypes, respectively

1.5.4 Autism Spectrum Disorder (ASD)

There is some overlap in symptomatology between AN and ASD, in regards to rigid and inflexible behaviours, cognitive processing (inefficient set shifting and weak central coherence) and social communication difficulties. The overlap in characteristics between AN and ASD was first reported by Christopher Gillberg (Gillberg, 1983; Gillberg, Gillberg, Råstam, & Johansson, 1996). Since these initial suggestions research in this area has been growing, with some suggesting that AN is the female presentation of ASD (Treasure, 2013).

Nilsson et al. (1999) reported that 16% of adolescents with AN in their sample (N=51) had a diagnosis of ASD, and this particular sub-group demonstrated poorer prognosis at follow-up. In a separate study Wentz et al. (2005) later reported that 23% of adults (N=30) with AN in their study met full diagnostic criteria for ASD.

Studies using self-report measures have also identified an association between AN and autistic traits. Baron-Cohen et al. (2013) found significantly elevated Autism Quotients (AQ (Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001)) in adolescents with AN compared to healthy control adolescents, as well as high systematising and low empathising scores, reflective of what is observed in ASD populations. Elevated AQ scores have also been demonstrated in the adult AN population (Hambrook, Tchanturia, Schmidt, Russell, & Treasure, 2008; Tchanturia et al., 2013c).

1.5.5 Personality disorders

Personality disorders frequently co-occur with AN (Dennis & Sansone, 1997; Rosenvinge, Martinussen, & Østensen, 2000), with the restrictive sub-type of AN being more commonly associated with obsessive compulsive personality features and the binge/purge sub-type more associated with features of impulsivity (Sansone, Levitt, & Sansone, 2004).

A systematic review demonstrated prevalence rates of ~22% for Obsessive Compulsive Personality Disorder (OCPD), ~19% for Avoidant Personality Disorder (APD) and ~10% Borderline Personality Disorder (BPD) for individuals with the AN restricting sub-type (Sansone et al., 2004). For individuals diagnosed with the binge/purge sub-type, the highest comorbid disorder was BPD (~25%), followed by avoidant or dependent personality disorder (~15%)(Sansone et al., 2004).

1.6 RISK FACTORS FOR ANOREXIA NERVOSA

AN is a complex and highly heterogeneous disorder, making the search for its underlying aetiology inherently difficult. The following section will aim to briefly summarise common known risk factors for AN (although not an exhaustive list). It is an impossible task to separate predisposing, precipitating and maintaining factors with regards to AN, as many factors are likely to match all three categories, Therefore they shall be discussed under the umbrella term 'risk factors'.

1.6.1 Genetics and heritability

A substantial amount of research into the biological underpinnings of AN has been conducted using family, twin and molecular genetic studies.

Family studies assess whether relatives of individuals with AN are at a higher risk of developing AN themselves. There is strong evidence from familial studies demonstrating that EDs aggregate in families, and the familial risk of both full and partial (sub-threshold) AN is high (Gershon et al., 1984; Strober, Freeman, Lampert, Diamond, & Kaye, 2014). The most recent family study indicated an elevated risk ratio for AN of 11.3 in first-degree relatives of probands, with a smaller risk ratio of 5.2 for partial AN, compared to never-ill control cases (Strober et al., 2014). This study also reported coaggregation and cross-transmission of EDs within families, whereby an AN proband increased the risk of BN by 3.5 times in a first-degree relative (Strober et al., 2014).

Unlike family studies, twin studies have the advantage of being able to separate out genetic and environmental influences on familial risk. Twin studies have estimated heritability rates of between 33 and 84% (Bulik et al., 2010; Klump, Miller, Keel, McGue, & Iacono, 2001; Kortegaard, Hoerder, Joergensen, Gillberg, & Kyvik, 2001), providing further evidence of an important genetic contribution in AN.

The search for candidate genes using molecular genetics has been slow and largely unsuccessful. Several genome wide linkage studies have produced inconclusive results (Bacanu et al., 2005; Devlin et al., 2002; Grice et al., 2002).
Three Genome Wide Association Studies (GWAS) have been conducted within the AN field and have struggled with recruiting the large sample sizes needed in these analyses to detect significance. Although the most recent GWAS study in AN failed to detect genome-wide significance, the results did highlight promising potential targets, suggesting that the sample was underpowered to detect significance (Boraska et al., 2014).

1.6.2 Prenatal risk factors

There is accumulating evidence to suggest that exposure to certain levels of sex hormones during the prenatal period can increase vulnerability to the development of an ED. In females in particular, decreased levels of testosterone in the prenatal developmental period have been associated with later ED psychopathology (Culbert, Breedlove, Burt, & Klump, 2008; Klump et al., 2006; Kothari, Gafton, Treasure, & Micali, 2014). Not all studies have replicated these findings (Baker, Girdler, & Bulik, 2012; Lydecker et al., 2012).

Evidence that maternal health during the prenatal period is a risk factor for AN in offspring has been inconsistent. Increased incidences of anaemia, diabetes and pre-eclampsia during pregnancy were observed in mothers of offspring with AN in one study (Favaro, Tenconi, & Santonastaso, 2006), whilst others have found evidence to suggest that maternal vitamin D deficiency during pregnancy predicted AN in offspring (Allen, Byrne, Kusel, Hart, & Whitehouse, 2013).

1.6.3 Perinatal risk factors

Obstetric complications are associated with increased risk across numerous psychiatric disorders (Jablensky, Morgan, Zubrick, Bower, & Yellachich, 2005). A systematic review and meta-analysis assessing obstetric complications as possible

risk factors for AN reported conflicting results. In a systematic review of 14 studies, some reported a significant association between birth complication and the later development of ED symptoms and others did not. A meta-analysis in the same review did not show any evidence of that instrumental delivery and prematurity were associated with ED risk, however the authors acknowledged that these findings could be due to insufficient statistical power (Krug, Taborelli, Sallis, Treasure, & Micali, 2013).

A larger Swedish register study demonstrated that smaller gestational age and other obstetric complications such as the umbilical cord being wrapped around the neck, breech delivery and delivery by caesarean, all increased risk for AN (Goodman, Heshmati, Malki, & Koupil, 2014).

1.6.4 Childhood and adolescence risk factors

Historically, emphasis was placed on puberty as a risk factor for AN in terms of the psychosocial factors (change in body, weight concerns etc.). Whilst this is likely to be an important factor, more recent research has emphasised the importance of the biological changes occurring during this developmental stage that may trigger the development of AN. Data from twin studies strongly suggest that both pubertal status and timing are crucial factors in AN, also implicating the activation of oestrogen. Heritability rates of ED symptoms rise from 0% in the prepubertal period to 50% at puberty (Klump et al., 2010).

1.6.5 Serotonergic system

Alterations to the serotonin (5-HT) pathway are hypothesised to play a role in the pathogenesis and maintenance of AN (Kaye et al., 2013). Findings from single photon emission computed tomography (SPECT) and positron emission tomography (PET) imaging studies show alterations to the 5-HT_{1A} and 5-HT_{2A} receptors and the 5-HT transporter in individuals with AN (Kaye et al., 2013). These alterations are present in currently ill and recovered individuals with AN, and may be related to the

high levels of anxiety, harm avoidance and distorted body image in AN (Kaye et al., 2013).

1.6.6 Psychosocial risk factors

Adverse life events such as childhood sexual abuse is associated with the development of AN; however, such experiences are not specific to ED and appear to be important in the pathogenesis of many psychiatric disorders.

There are a number of environmental factors thought to be important in the development of AN. Dissatisfaction or concerns with weight and shape, overvaluation of the thin ideal, and weight-related teasing can encourage and trigger dieting behaviour, increase the risk of AN (Johnson & Wardle, 2005; Stice, Ng, & Shaw, 2010). Negative emotional affect, such as anxiety or depression has also been implicated as a trigger for pathological eating behaviours, such as vomiting (Stice et al., 2010).

Personality traits such as perfectionism, neuroticism and obsessive-compulsive personality traits have also been implicated as risk factors (Lilenfeld, 2011). In addition to this, perceived social rank, social comparison and related emotions such as self-esteem and shame, have also been marked as important aetiological risk factors for AN. Troop, Allan, Treasure, and Katzman (2003) found that women with EDs reported a more unfavourable social comparison than HC women, and levels of social comparison were related to the severity of ED symptoms. Troop and Connan (2003) have also suggested a biological mechanism, whereby social rank is likely to be associated with weight loss due to appetite suppression via a dysregulated serotonin system. A later study by Troop, Allan, Serpell, and Treasure (2008) also found that levels of shame were significantly associated with ED pathology. Furthermore, shame as a measure of perceived subordination was specifically associated with symptoms of AN, whereas shame as a measure of feelings was more associated with symptoms of BN. These findings highlight the important role that social rank and comparison are likely to play in the aetiology of the different EDs (Troop et al., 2008; Troop et al., 2003).

Historically, parenting style had been implicated as playing a causal role in the development of EDs (Bruch, 1982). However, it is now commonly accepted that whilst different parental styles and behaviours may serve to maintain EDs (Goddard et al., 2011), they represent a non-shared risk factor for AN (Karwautz et al., 2011) and not a causal one.

A recent study assessing a new socio-cultural model of EDs highlighted that whilst socio-cultural factors such as peers, family and the media are likely to be important in the development of EDs, it is likely that they work in different way across different ED sub-types (Krug et al., in press). Krug et al. (in press) found that perceived influences from peers and family were associated with EDNOS, whereas a verbally abusive parenting style was more associated with the AN-binge/purge sub-type.

1.6.7 Genetic and environmental interplay

The aetiology of AN is likely to be due to a complex interaction between genetic vulnerability and environmental factors, with twin studies estimating its pathogenesis to be 60% genetic factors and 40% environmental factors (Bulik et al., 2006).

In a discordant sister-pair design Karwautz et al. (2001) demonstrated that an interaction between both intrinsic factors, such as personality traits, and extrinsic factors like parental expectations, increased the risk for AN. Furthermore, Karwautz et al. (2011) also explored the gene-environment interaction in AN in 128 discordant sister pairs. There was a significant interaction between environmental risk factors such as problematic parenting and a polymorphism of the serotonin transporter gene (5-HTTLPR). These findings suggest that the aetiology of AN is multifactorial and maintenance models should therefore consider both intrinsic and extrinsic factors.

1.7 MAINTENANCE MODELS OF ANOREXIA NEROVSA

Relevant maintenance models for AN that take into account the risk factors described above and are in line with the context of this thesis are summarised in the following section.

1.7.1 The neurodevelopmental model (Connan, Campbell, Katzman, Lightman, & Treasure, 2003)

Connan et al's. (2003) neurodevelopmental model considers the aetiology of AN to be multi-factorial, incorporating genetic vulnerability, perinatal stressors, dysregulation of biological systems, and poor cognitive and socio-emotional functioning. The theoretical model proposes that an existing genetic predisposition interacts with perinatal stressors, such as birth prematurity or trauma and anxious/insecure attachment styles, to produce modifications to biological brain systems, such as the Hypothalamic Pituitary-Adrenal (HPA) axis. These changes, together with an overactive serotonergic system, result in dysregulated stress responses throughout life. Perinatal factors such as attachment style and poorly regulated stress response can also disrupt the typical development of cognition and socio-emotional processing, further increasing the stress response. Profound metabolic changes and changes to the endocrine system during puberty heighten the susceptibility to developing AN, providing some explanation for the increased incidence rates in adolescent females.

1.7.2 The biopsychosocial model (Southgate, Tchanturia, & Treasure, 2005)

This model considers recent neuroscientific evidence in the underpinnings of EDs.
It postulates that early life experiences such as birth complications and abnormal feeding act as vulnerability factors for AN, and stressful life events can trigger dieting and exercise behaviour leading to nutritional stress.

The model's central focus is on potential changes in brain function during adolescence that may increase the risk of AN, and places emphasis on two important components. Firstly, the model proposes that high emotional distress related to a poorly modulated stress response (Connan et al., 2003) and a compromised nutritional state disrupts normal brain maturation (such as synaptic pruning and myelination). This in turn interferes with reward pathways.

Secondly, the authors implicate 'the social information processing network' in both the development and maintenance of EDs. They posit that disturbances to the maturational process, along with pubertal hormonal changes, impact on this system and cause a hypersensitivity to certain emotional stimuli, which manifests as the socio-emotional difficulties frequently observed in the disorder. The development of higher order cognitive functions takes place after these pubertal changes, and therefore an immature cognitive processing system is unable to regulate such a heightened response to social stimuli. This results in some of the phenotypic behavioural characteristics observed in AN, such as rigidity and detail-biased processing. Lastly, the model also considers certain personality traits, such as perfectionism and over-control to be important in the manifestation of the phenotypic characteristics of AN. The authors argue that on the basis of these neuroscientific underpinnings, treatments should aim to specifically target both the social and cognitive systems.

1.7.3 Transdiagnostic cognitive behavioural model (Fairburn, Cooper, & Shafran, 2003).

This transdiagnostic model proposes that all EDs share the common underlying maintaining factor of overvaluation of the control of weight and shape. As a consequence of this key factor, other pathological eating disorder-related behaviours are triggered such as self-starvation, excessive exercise, purging and laxative use. Interpersonal difficulties and mood dysregulation are also considered to contribute to the maintenance of the disorder.

1.7.4 The cognitive interpersonal maintenance model (Schmidt & Treasure, 2006; Treasure & Schmidt, 2013)

The cognitive interpersonal maintenance model of AN is also a multifactorial model. It posits that there are four factors acting as both predisposing and maintaining factors for the disorder (Fig 2). Firstly, a thinking style characterised by premorbid Obsessive Compulsive Personality traits (OCPT) such as perfectionism and rigidity act as a vulnerability factor, and are manifested by a specific cognitive processing style, involving cognitive inflexibility (poor set shifting) and poor global processing with a preference for details (weak central coherence). The model suggests that such characteristics render individuals susceptible to AN, for example, an inflexible thinking style with focus on details results in rigid rule following (obsessive dietary rules). A vicious cycle ensues as rapid weight loss and starvation cause further inflexibility and poor global processing by the brain. As these traits appear to be familial the model suggests that this can cause maladaptive responses to the illness within families, such as high expressed emotion and serve to maintain the ED. Secondly, an emotional style characterised by high levels of avoidance and difficulties with regulating and processing emotions, further predispose and maintain ED behaviours. Thirdly, the model also implicates proanorexic thinking, suggesting that perceived benefits of the illness foster ambivalence toward treatment and recovery. Lastly, difficulties with interpersonal relationships, for example with family members, can result in behaviours that may inadvertently maintain ED behaviours.

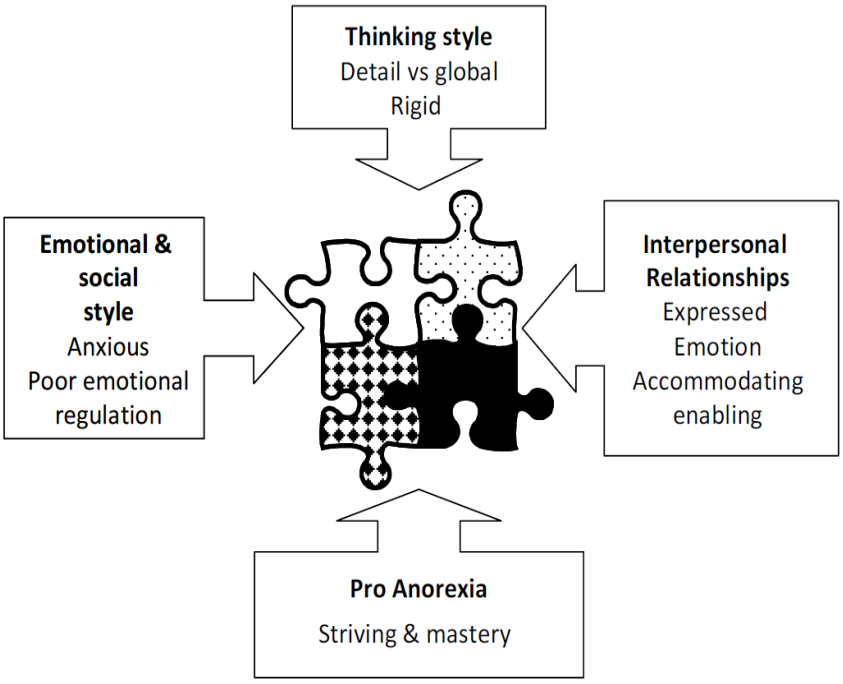

Figure 2: The Cognitive Interpersonal Model of AN (Treasure & Schmidt, 2013)

1.7.5 The integrative neuroscience model (Hatch et al., 2010a)

This model is built on the premise that a motivation to reduce perceived threat drives human behaviour. The authors posit that disturbed emotion processing is central to the disorder. A genetic vulnerability to abnormal processing of danger cues leads to heightened processing of negative emotions, impacts on the way emotions are experienced, and disrupts cognitive processes. Stressful life events may trigger food avoidance as a way of regulating negative emotional responses and decreasing perceived danger. This can lead to conditioning, whereby food becomes associated with danger and restriction is associated with reward (particularly in individuals where food was already less rewarding). These associations lead to starvation, whereby depression, obsessionality and cognitive difficulties are exacerbated and serve to maintain the disorder.

1.7.6 A staging model (Treasure, Stein, & Maguire, 2014)

This model suggests that there are stages in the development of AN psychopathology: High risk, prodromal, full syndrome and severe and enduring. The model suggests that treatments should be matched to the stage of illness, with treatment prognosis becoming poorer over the stages. The model also considers neuroprogression, suggesting that prolonged starvation and malnourishment can impact on social difficulties and cause changes in brain anatomy and function, accounting for treatment complications in the severe and enduring stage of illness.

The authors posit that during child and adolescence individuals may become exposed to certain vulnerability factors including social difficulties and OCPD traits (cognitive rigidity, poor global processing). These risk factors can lead to the development of subclinical symptoms (prodromal stage). If these symptoms do not remit the individual can transition into the full syndrome stage. The severe and enduring stage is characterised by prolonged illness over a period of seven years or more.

1.7.7 Aberrant habit formation model (Walsh, 2013).

This model considers the broader context of learning in an attempt to explain how dieting behaviours become established and persistent. It draws on research from both animals and humans in the study of addictions. It suggests that these behaviours become established and entrenched through the two distinct learning processes of action-outcome and stimulus-response learning. Action-outcome learning (also termed instrumental or operant conditioning), is important in the formation of new behaviours and occurs when a behaviour is linked to a reward. It is a reward-sensitive process: as the paired reward decreases, so will the linked behaviour. Over time, the behaviour will become less sensitive to the reward if it continues to be rewarded, and this forms the basis for stimulus-response learning or habit formation (Balleine & O'Doherty, 2010).

The model posits that in regard to AN, dieting behaviour starts as goal-directed behaviour that leads to weight loss, a highly rewarding outcome. The behaviour then becomes persistent and repetitive, and habitual. Once the habitual behaviour is established it becomes more resistant to change. The model also suggests that rewards are more salient in adolescence due to developmental brain changes. As inhibitory control areas of the brain are still underdeveloped during this time this type of learning is particularly pertinent, and accounts for the increased vulnerability of AN during adolescence.

1.7.8 Summary of maintenance models

The above models implicate multiple factors in the causation and subsequent maintenance of AN. AN is a highly heterogeneous disorder and it is therefore a challenge to elucidate its precise aetiology. It is clear from these models that common underlying mechanisms, such a cognitive styles and socio-emotional processing are important factors in the pathogenesis and maintenance of AN. Further research in this area could make a significant contribution to our understanding of these features and yield new treatment targets for the disorder.
The following section will provide an overview of the literature in regards to our current understanding of neuropsychological (set shifting and central coherence) and socio-emotional processing in AN, in order to inform the specific aims and hypotheses of this thesis.

1.8 NEUROPSYCHOLOGICAL PROCESSING IN ANOREXIA NERVOSA

The chronic course and associated psychosocial impairment, as well as the high mortality rates of AN highlight the need for the development of more effective treatments. Treatments targeting overt ED pathology have thus far produced disappointing outcomes for AN. This has spurred investigative interest in underlying mechanisms likely to be important in the pathogenesis of the disorder that could offer insights into the aetiology of AN and provide new and empirically informed targets for treatments.

Clinical observations of behavioural inflexibility and detail-focused thinking in AN patients sparked interest in hypothesis-driven research investigating these specific aspects of cognitive processing in AN, namely that of set shifting and central coherence.

Set shifting is an executive function that can be defined as the ability to switch flexibly between sets, rules and behaviours (Lezak, Howieson, Bigler, & Tranel, 2012). The ability to set shift is crucial for both cognitive and behavioural flexibility, and will impact on an individual's ability to successfully react and adapt to a constantly changing environment. Set shifting has been implicated as an important factor across a range of psychiatric disorders. There is evidence of poor set shifting abilities in OCD (Head, Bolton, & Hymas, 1989), ASD (Hill, 2004), and Schizophrenia (Pantelis et al., 1999). There is also a body of evidence to suggest that cognitive flexibility is important for health and wellbeing in general (Kashdan & Rottenberg, 2010). Prominent models have placed cognitive and behavioural flexibility as a core feature of AN, suggesting that a fear of harm and novelty avoidance lead to heavy reliance on rules to guide behaviours (Zucker, Herzog, Moskovich, Merwin, & Lin, 2011).

Central coherence is described as the tendency to process information in a holistic and contextual way (Frith, 1989; Happé, 2013). On the other hand, a tendency for detail-focused processing at the expense of global context is referred to as Weak Central Coherence (WCC,. (Booth, 2006)). Central coherence is assessed along a

continuum, with global and holistic processing lying at one end of the spectrum and detail-focused processing at the opposite end.

A heavily detail-focused cognitive style can be problematic, impacting on the individual's ability to draw meaningful context from the details. WCC is probably most widely associated with neurodevelopmental disorders such as ASD (Happé, 2013). The observation of the similarities in phenotypic characteristics between individuals with ASD and AN ignited interest in the concept of WCC in AN (Gillberg, 1983; Lopez, Tchanturia, Stahl, & Treasure, 2008b).

1.8.1 Set shifting in adults with AN

A rigid and inflexible behavourial style is associated with the phenotypic characteristics of AN (Zucker et al., 2011). The familiar clinical picture of, for example, stringent and inflexible adherence to food-related routines and rituals is hypothesised to be underpinned by difficulties in set shifting. Neuropsychological studies within the AN field have supported this notion, and have consistently demonstrated that adults with AN perform poorly on measures of set shifting in comparison the HCs (e.g. (Roberts, Tchanturia, Stahl, Southgate, & Treasure, 2007; Wu et al., 2014)).

The most widely used neuropsychological measure of set shifting in psychiatry, and certainly the most reported measure within the ED field is the Wisconsin Card Sorting Test (WCST, (Heaton, 1993)). Historically, this task was administered manually with a deck of cards, but its computerised version, which minimises experimenter error, is now often the preferred option in more recent studies. In this task the participant is required to match a stimulus card to one of four category cards, by an unknown sorting rule. Each time the participant makes a sort the computer offers feedback on whether they have sorted the card correctly or incorrectly. The participant must use this feedback to ascertain what the sorting rule is. After so many correct sorts, the sorting rule changes unpredictably and the participants must now abandon the redundant sorting rule and shift their behaviour in order to decipher the new sorting rule. Each time the participant continues to

abide by the old sorting rule, it is termed a perseverative error, and this is the main outcome for measuring set shifting abilities. A higher number of perseverative errors indicates poorer set shifting.

There is a wealth of evidence from the WCST demonstrating that adults with AN perform significantly more perseverative errors compared to HC groups (Abbate-Daga et al., 2011; Fassino et al., 2002; Galimberti et al., 2013; Koba, Shrie, & Nabeta, 2002; Nakazato et al., 2010; Pignatti & Bernasconi, 2013; Steinglass, Walsh, & Stern, 2006; Tchanturia et al., 2012b; Thompson, 1993). Tenconi et al. (2010) also reported a significantly higher number of perseverative errors. However, this study included both children and adolescents with AN and adults with AN (age range: 14-47 years), and did not provide separate means and standard deviations. Two studies, however, did fail to find differences between AN adults and HC adults (Giel et al., 2012; Ohrmann et al., 2004). It is possible that both of these studies were under-powered to detect statistic differences, and Giel et al. (2012) based their power calculation on data from females with depression and not anorexia.

The largest experimental study in the field compared the performance of 171 participants with AN on the WCST to 199 matched HCs and found a significantly higher number of perseverative errors in the AN group compared to HCs with large effect sizes (AN inpatients d=1.00, AN outpatients d=0.8, (Tchanturia et al., 2012b))
A recent meta-analysis by Tchanturia and Lang (2014) of set shifting in adults with AN demonstrated a pooled effect size of 0.6 when observing WCST performance.
Poor set shifting in adults with AN have also been observed across a number of other neuropsychological tasks including the Trail Making Task (TMT, (Delis, Kaplan, & Kramer, 2001))(Jones, Duncan, Brouwers, & Mirsky, 1991; Kingston, Szmukler, Andrewes, Tress, & Desmond, 1996; Mathias & Kent, 1998; Tchanturia et al., 2004c; Tenconi et al., 2010; Thompson, 1993; Witt, Ryan, & Hsu, 1985), the Haptic illusion task (Tchanturia et al., 2004a; Tchanturia, Morris, Surguladze, & Treasure, 2002; Tchanturia, Serpell, Troop, & Treasure, 2001; Uznadze, 1966), and the Brixton (Burgess & Shallice, 1997; Tchanturia et al., 2004a). Stedal, Rose, Frampton, Landrø, and Lask (2012) did not find any significant differences on the TMT or the Brixton. However, their sample was inclusive of children and adolescents and adults with AN (age range: 9.5-27.1 years), and this may explain the null findings.

Only one study has investigated set shifting in males with AN, also reporting significantly higher levels of perseveration on the WCST and TMT (Goddard, Carral-Fernández, Denneny, Campbell, & Treasure, 2014). The limited number of studies examining cognitive processing in males with AN highlights the need for further research in this area.

There is also evidence of inefficient set shifting in weight-restored individuals, albeit in an intermediate form (Lindner, Fichter, & Quadflieg, 2014; Roberts, Tchanturia, & Treasure, 2010; Tchanturia et al., 2012b). These studies suggest that inefficient set shifting in AN may not be entirely consequential of starvation, but that it is perhaps an underlying characteristic that is then worsened and exacerbated by starvation and malnutrition.

There is therefore consistent evidence that adults with AN show difficulties with set shifting. The difficulties observed in AN are subtle and cannot be described as 'deficits' or 'impairments'. However in relation to intelligence quotient (IQ), which is typically above average in AN (Lopez, Stahl, & Tchanturia, 2010), the processing style is certainly sub-optimal, and therefore the term 'inefficiencies' is a more accurate description to capture the nature of the difficulties. Therefore, from herein in this thesis the term 'inefficiencies' will be used to describe these difficulties.

1.8.2 Set shifting in unaffected AN relatives

There is also significant experimental data to suggest that inefficient set shifting is an inherited vulnerability in AN (Galimberti et al., 2013; Roberts et al., 2010).
A majority of this work has examined unaffected sisters of those with AN, and has demonstrated that inefficient set shifting occurs at a higher rate in groups of unaffected AN sisters than HCs. Galimberti et al. (2013) also found higher presence of this trait in a small group of unaffected mothers; however, this study included a mixed group of unaffected mothers and sisters, and so the effect sizes of mothers alone could not be determined.

The designs of these studies do not discriminate between genetic and environmental influences on set shifting. However, preliminary results from the only available genetic study of set shifting in AN demonstrated high concordance rates of inefficient set shifting in both monozygotic and dizygotic twins, strongly suggesting a genetic component (Kanakam, Raoult, Collier, & Treasure, 2013).

Combined evidence of inefficient set shifting in currently ill and recovered AN, its presence in unaffected family members and results from twin studies has led to the hypothesis that it may represent an underlying trait in AN. However, the ED field also needs confirmation of the set shifting abilities of children and adolescents with AN. Evidence of its presence in younger populations would add further clarity to its status as an underlying trait, as theoretically the effects of starvation on neuropsychological processing in individuals with shorter illness durations should be less pronounced. The next section will therefore outline the literature in regards to our current knowledge of set shifting in children and adolescents with AN.

1.8.3 Set shifting in children and adolescents with AN

EMPIRICAL ARTICLE

Set Shifting in Children and Adolescents with Anorexia Nervosa: An Exploratory Systematic Review and Meta-Analysis

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ABSTRACT

Objective: Set shifting inefficiencies in adults with anorexia nervosa (AN) are established, however the neurocognitive profile of children and adolescents with AN is less clear. This study aimed to provide a review of the literature.

Method: Electronic databases were used to search for manuscripts.

Results: Meta-analysis was performed on seven studies using two neuropsychological tests (Trail Making Task, TMT; Wisconsin Card Sorting Task, WCST). The mean difference in outcome between AN and healthy control (HC) groups was standardized by calculating Cohen's *d*. Meta-analysis of TMT studies showed a nonsignificant negative, pooled standardized mean difference of −0.005 (95% C.I. −0.416 to 0.406, $z = 0.02$, $p = .98$). WCST studies revealed a nonsignificant pooled effect size of $d = 0.196$ (95% C.I. −0.091–0.483, $z = 1.34$, $p = .18$). Studies which did not allow for a calculation of effect size typically showed a nonsignificant, worse performance by the AN groups.

Discussion: The inefficiencies in set shifting that are apparent in the adult AN literature do not appear to be as pronounced in children. This may suggest that set shifting difficulties in adult AN are the result of starvation or indicative of longer duration of illness. Larger studies are needed to confirm these impressions. © 2013 Wiley Periodicals, Inc.

Keywords: anorexia nervosa; adolescent; set-shifting; cognitive flexibility; thinking style; executive function

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Introduction

Recent research in anorexia nervosa (AN) has highlighted inefficient cognitive processing across a number of executive functions, relative to IQ. In particular, adults with AN show problems in set shifting (SS),[1,2] that is the ability to move flexibly from one task/strategy to another.[3] Poor SS has been reported in individuals with a past history of AN, who have achieved remission,[4] and in unaffected sisters of those with eating disorders.[5] It is speculated that it could be a possible endophenotype for AN, however, consistent evidence of premorbid inefficiencies in this population is lacking. Without evidence from children, it is impossible to determine whether these difficulties are truly a predisposing factor or a neurological "scar" of starvation. Conducting neuropsychological investigations in younger populations is advantageous, as the shorter duration of illness will increase the chances that "scars of starvation" will be less pronounced. This systematic review aims to summarize the literature on SS in children and adolescents with AN.

Method

The meta-analysis was conducted according to the "PRISMA statement" (preferred reporting items for systematic reviews and meta-analysis).[6]

Eligibility Criteria

Studies using neuropsychological measures of SS to assess children and adolescents with AN were included. Eligibility criteria included (1) diagnosed with AN; (2) children and adolescents (aged 10–18); (3) published in English.

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Information Sources and Search

Electronic databases were searched, including Scopus, Psychinfo, Medline and Web of Science. Journals were searched up to/including September 2013. Search terms included: Anorexia Nervosa, set shifting, cognitive flexibility, cognitive rigidity, neuropsychology, executive functions.

Selection

Each study's title and abstract were screened by the first author (KL) and the principle author (KT). Relevant studies were retrieved and full text articles were assessed further.

Summary of Measures

The following neuropsychological measures of SS were used in the studies included in this review:

Wisconsin card sorting test (WCST[3])

The trail making task (TMT[3])

The Brixton task [3]

Intra/extra dimensional set shift subtest[7]

Color-word interference test[3]

Verbal fluency test[3]

Groton–maze learning task[8]

Switching of attention test[9]

The category learning task[10]

Visual set-shifting task[11]

Synthesis of Data

Means and standard deviations for AN and Healthy Control (HC) groups were taken from each manuscript. The mean difference in outcome between AN and HC groups was standardized by calculating Cohen's *d*, the difference between two raw means divided by the pooled standard deviation.[12] Positive effect sizes mean that the HCs performed better than the AN. The standard error of each study's standardized effect size was calculated from the estimated effect and the group sizes.[13]

Meta-analyses were only performed on studies using the TMT and WCST, as the number of studies using each of the other neuropsychological tests was insufficient. These studies are therefore commented on individually.

The meta-analyses for the TMT and WCST were done by pooling standardized effect sizes using a random-effects model. This model assumes that as well as within-group variability of scores (due to sampling error), variability of mean effect sizes is also caused by differences of the effect between studies (between-study heterogeneity). Random-effects models incorporate the between-group heterogeneity, resulting in estimates with wider confidence intervals than fixed-effects models. However, the random effects models are thought to be more realistic in psychiatric studies due to the variety of patient groups from different populations (i.e., studies from different countries or with different age distributions) and due to different experimental settings.[12] Because of the number of studies employing the TMT and WCST, a formal assessment of the assumption of homogeneity of true effect sizes was not possible. Analyses were carried out in STATA 11 (StataCorp, College Station, TX) using the user-contributed *metan* command for meta-analyses.[14]

Results

Nine appropriate studies were identified and included in the review. All studies included AN and HC groups (see **Table 1**). Psychiatric and HC samples were matched for age and IQ. Participants in AN groups met DSM-IV criteria, with the exception of Allen et al.[20] whose sample included AN, BN and EDNOS. Statistically significant results are more likely to be published than nonsignificant results. The presence of publication bias is usually assessed informally by visual inspections of funnel plots.[24] The number of studies did not allow us to perform such an assessment. However, most published studies showed nonsignificant results (see below), suggesting that publication bias should be not a concern.

Of the nine studies identified in this review, meta-analyses were performed on seven studies using the TMT ($N = 4$ studies) and WCST ($N = 3$ studies). The remaining studies are commented on individually ($N = 4$ studies). A number of methodological flaws in the existing literature were identified in this review, all of which are important to discuss as a caveat to the results. The most challenging of these problems was the number of different neuropsychological tests currently being used to study SS in AN. We found nine different tests used in 11 studies, resulting in only two tests (TMT and WCST) being included in meta-analyses. There also were inconsistencies in the versions of tests being used (i.e., using a 64-card version of WCST instead of the 128-card version). Moreover, studies using the same tests were inconsistent in their reported outcome measures (e.g., for the WCST reporting perseveration errors as a measure of SS), making comparisons between studies difficult. Finally, many recruited small samples and lacked information regarding comorbidities, medication use, and task administration procedures, all of which made assessing the quality of the studies difficult. Nonetheless, it was possible to draw conclusions and make future recommendations from this appraisal of the literature.

Trail Making Test (TMT)

The TMT was used in four studies (**Fig. 1A**).[16,17,22,23] The Frampton et al.[23] study is

TABLE 1. Participant demographic information for included studies

Author/date	Group	*N*	Age	BMI	Medication	Comorbidities	Length of Illness (Months)	Test Used
Hatch et al. (2010)	AN	37	15.16 (1.63)	16.1 (0.9)	—	—	9.74 (10.11)	IntegNeuro
	HC	45	—	—	None	None		
Sarrar et al. (2011)	AN	30	16.2 (1.2)	15 (1.2)	—	Five affective disorder; 2 OCD	—	TMT
	HC	28	16.7 (1.3)	20.5 (2.5)	None	None		
Andres-Perpina et al. (2011)	AN	37	15.4 (1.5)	15.3 (1.4)	—	None	—	TMT; WCST; Stroop
	HC	41	15.4 (1.5)	—	None	None		
McAnarney et al. (2011)	AN	24	16.3 (1.2)	16.7 (1.3)	None	None	—	WCST; CANTAB/IED
	HC	37	15.9 (1.5)	22.3 (3.7)	None	None		
Buhren et al. (2012)	AN	28	15.5 (1.5)	15.4 (1.2)	—	—	—	Amsterdam Neuropsychological
	HC	27	14.9 (1.5)	21.0 (2.8)	None	None		
Allen et al. (2012)	AN	58	17.5 (0.26)	24.78 (8.10)[a]	—	—	—	CogState; Groton maze learning task
	HC	542	16.98 (0.24)	22.55 (5.09)	None	None	—	
Shott et al. (2012)	AN	15	14.8 (1.1)	16.2 (1.1)	—	—	9 (8)	Category learning task
	HC	16	14.0 (1.6)	20.5 (2.2)	None	None	—	
Fitzpatrick et al. (2012)	AN	32	14.93 (1.88)	—	—	—	—	WCST; TMT; verbal fluency; color–word interference; Brixton
	HC	22	15.40 (1.89)	—	None	None	—	
Frampton et al. (2012)	AN	15	19 (1.95)	W/H ratio 88.13 (10.15)	—	—	—	TMT; verbal fluency test; color–word interference
	HC	15	18.3 (2.20)	106.39 (13.80)	None	None	—	

Notes: *N* = number of participants, BMI = body mass index (BMI; kg m^{-2}), WCST = Wisconsin card sorting task, TMT = trail making task.
[a]This sample is inclusive of AN, BN, and EDNOS participants.
[b]This study is separated into two cohorts in the meta-analysis based on brain function.

presented as two separate studies, as the AN sample was divided into two subgroups. The subgroups were based on neurobiological status reflecting results from a brain scan that measured regional cerebral blood flow (rCBF). In this study there was a "hypoperfusion" group that was characterized by inter-hemispheric rCBF asymmetry, and a normal perfusion group where such inter-hemispheric rCBF asymmetry was not present (see Ref. 20 for full details). A random effects meta-analysis of all of the TMT studies (total $N = 220$, 114 AN, 106 HC) revealed a non-significant negative pooled standardized mean difference of $d = -0.005$ [95% C.I. −0.416–0.406, $z = 0.02$, $p = .981$, $I^2 = 50.5\%$].

Wisconsin Card Sorting Test (WCST)

The WCST was employed by three studies (**Fig. 1B**).[17,18,22] The random-effects meta-analysis with a total sample size of 193 (AN: 93, HC: 100) revealed a non-significant pooled effect size of $d = 0.196$ [95%C.I> −0.091–0.483, $z = 1.34$, $p = .18$].

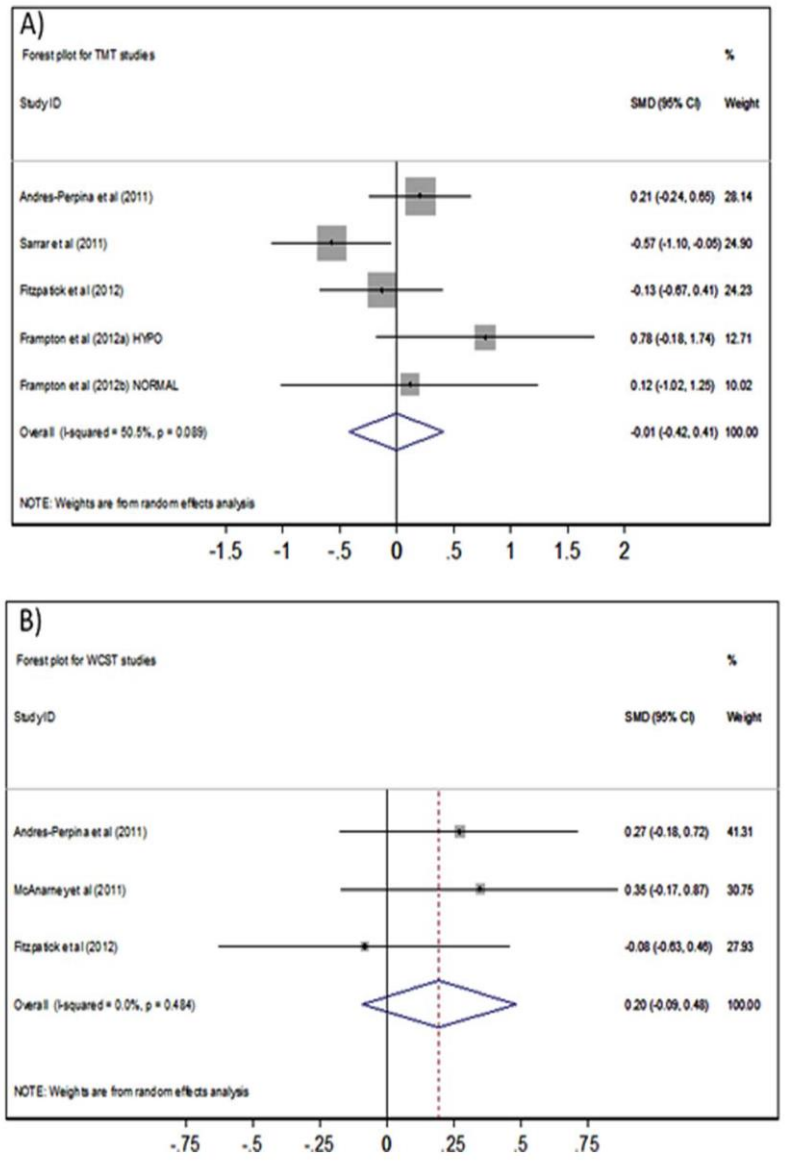
Results from other Neuropsychological Measures of Set Shifting

Significant differences in performance between the AN and HC group (with AN showing more perseveration) were found on the Groton Maze Learning Task[15] ($d = 0.42$ [95% C.I: 0.14, 0.7], $p < .05$), and the Brixton Task (hypoperfusion group versus HC $d = 0.78$ [95% C.I: −0.2, 1.76]).[23] However, no significant differences were found between the AN and HC groups on the Brixton Task[22] ($d = 0.47$ [95% C.I: −0.09–1.03] $p = .135$), the IED[18] ($d = 0.12$ [95% C.I: −0.4, 0.64] $p = .661$), the color–word interference[22] ($d = 0.17$ [95% C.I: −0.38, 0.72] $p = .573$,[23] normal perfusion AN group vs. HCs $d = 0.13$ [C.I: −1.03, 1.29]), the Verbal Fluency Test[22] ($d = 0.05$ [95% C.I: −0.05, 0.6] $p = .854$[23]; hypoperfusion group vs. HCs [$d = 0.17$, N.S], normal function group vs. HCs [$d = 0.54$, N.S]), the Switching of Attention Test[21] ($d = 0.2$ [95% C.I: −0.24, 0.64] $p = .073$), the category learning test[19] ($d = 0.3$ [95% C.I: −0.42, 1.0] $p = .083$), or the Visual Set-Shifting Task[16] ($d = 0.68$).

Discussion

The aim of the present study is to provide a synthesis of the existing literature of SS abilities of children and adolescents with AN. A number of methodological constraints were highlighted, including the variety of neuropsychological tests being used to measure SS, inconsistencies in data outcome reporting (making studies incomparable), small sample sizes, and lack of reporting of medication use and comorbidity. These study

Figure 1 Forest plots for (A) trail making task (TMT) studies, (B) Wisconsin card sorting test (WCST) studies. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]



limitations make interpretation of the data challenging. However, given the consistency of the available data, it was possible to draw conclusions.

The meta-analyses that were performed on the TMT and WCST suggest that the inefficiencies apparent in adult AN may not be present to the same extent in the child and adolescent population. Systematic reviews of the adult literature have reported small-to-medium effect sizes for the WCST and TMT,[25] and large empirical studies in the adult literature using the WCST[2, 4] have consistently demonstrated inefficiencies in SS in AN. Research into cognitive inefficiencies in the child and adolescent population is in its early stages, and therefore the findings of no significant differences between AN and HC in this exploratory review should be interpreted with some caution. The large confidence intervals of the effect sizes for TMT and especially WCST in these studies overlap with reported confidence intervals of the effect sizes for adults reported by Roberts et al.[25] suggesting that more research needs to be done to demonstrate that performance does differ significantly between children/adolescents and adults. Moreover, although group differences were not significant, children with AN typically showed poorer

performance than HCs. Small differences in SS abilities may hint that although SS inefficiencies may not be as marked as in adults, there may be an underlying cognitive disturbance that becomes exacerbated by starvation and contributes to the maintenance of AN and neurological scar effects after recovery. Supporting this, neuroimaging studies have consistently shown structural abnormalities in multiple brain regions in adults with AN,[25] which may contribute to disturbances in SS performance and/or reflect the consequences of long-term starvation. Such structural neuroimaging studies are yet to be carried out with adolescents with AN and due to maturational brain changes they may not provide much insight. However, functional imaging studies with adolescents could be useful. For example the use of functional maps from a flexibility task at different stages of illness could provide functional markers of differing illness trajectories (i.e., delineating chronic cases from those who are more likely to recover) and therefore help to predict treatment outcomes.

It is important to consider the typical developmental trajectory of SS abilities when assessing our results. A meta-analysis by Romine and Reynalds[26] assessed the development of frontal-lobe functioning through the examination of numerous neuropsychological tasks, including SS using the WCST. Results from five studies suggested that the greatest period of development for SS occurs between 5 and 8 years of age (large effects sizes) with a moderate amount of development occurring between 11and 14 (small-medium effect sizes). Development was less prominent after those periods. As a majority of the studies included in the present review included mid-late adolescents, we would expect SS ability to be fully developed, meaning that any SS inefficiencies (even those of small effect) are unlikely to be due to differences in cortical development between participants in different studies. Nonetheless, the interaction between rapid brain maturation (e.g., synaptic pruning and myelination) and pubertal progress (the role of gonadal steroid hormones[27]) with individual differences in clinical characteristics (age of onset, severity) in the samples cannot be underestimated and provides further interpretative challenges, as this could affect each individual's performance idiosyncratically. Such potential differences in brain development could therefore eradicate any significant effects.

To our knowledge, this study is the first to attempt a synthesis of findings relating to SS abilities in children and adolescents with AN. Our exploratory review therefore represents the first steps in attempting to clarify the neurocognitive profiles of children/adolescents with AN. Results hint that SS inefficiencies are less pronounced in children/adolescents as compared to adults. However, it is also clear that larger, more robust studies are needed to clarify the neuropsychological status of young people with AN. Clinically, cognitive remediation therapy (CRT) for adult AN is gaining evidence,[28] and there are attempts to apply the same treatment approach to adolescents.[29] Defining target areas in children/adolescents with AN is important because if SS inefficiencies are not present in younger AN patients, then CRT directly targeting cognitive flexibility becomes questionable. To help clarify these issues, future research would benefit from assessing larger samples of children and adolescents with AN, using the same neuropsychological tests (i.e., findings suggest that the TMT and WCST may be the best measures of SS), and consistently reporting the same outcome measures from these tests (e.g., reporting perseverative errors from WCST).

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Since the publication of this review there has been two further study investigating set shifting in children and adolescents with AN. Kjaersdam Telléus et al. (2014) reported no differences in performance on the TMT or the Intra-Extra dimensional shift task between AN and HC groups. The AN participants in the study were of early onset (~12 months) and this study also included males and females. These inclusion criteria may have contributed to the null finding in this study. Stedal and Dahlgren (2015), reported no significant differences in mean Z scores for the TMT between AN and HC groups. Participants for this study were recruiting from in and outpatient setting and were undergoing different intensities of treatment at the time of testing. This may have impacted on the study's outcome. Participants for this study were recruiting from in and outpatient setting and were undergoing different intensities of treatment at the time of testing. This may have impacted on the study's outcome.

1.8.4 Central Coherence in adults with AN

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REVIEW ARTICLE

Central coherence in eating disorders: An updated systematic review and meta-analysis

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Abstract

Objectives. A bias towards local information over the global "gist" (weak central coherence, WCC), has been identified as a possible contributing and maintaining factor in eating disorders (ED). The present study aimed to provide an updated review of the WCC literature and examine the hypothesis that individuals with ED have WCC. *Methods.* The new search found 12 eligible studies. Meta-analyses were performed on nine of these 12 studies, the remaining three were commented on individually. Data were combined with data from the previous 2008 review, and meta-analyses were performed on 16 studies (nine studies from the new search and seven studies from 2008 review). *Results.* Meta-analysis of the Group Embedded Figures Task provided evidence of superior local processing across all ED subtypes (pooled effect size of $d = -0.62$ (95% CI = −0.94, −0.31), $P < 0.001$). Evidence of poorer global processing in ED groups was found from meta-analyses of the Rey-Osterrieth Complex Figures task ($d = -0.63$ (95% CI = −0.77, −0.49, $P < 0.001$), and the Object Assembly Task ($d = -0.65$ (95% CI = −0.94, −0.37), $P < 0.0001$). *Conclusions.* As well as supporting the results of previous studies by providing evidence of inefficient global processing, this review has provided evidence of superior local processing, which supports the WCC hypothesis in ED.

Key words: *eating disorders, anorexia nervosa, bulimia nervosa, central coherence, global processing*

Introduction

Anorexia nervosa (AN) is characterised by problems with eating, weight and shape that often develop in the context of obsessive compulsive and perfectionistic personality traits (Wade and Tiggeman 2013). These personality traits are associated with a poorer prognosis (Crane et al. 2007; Sauro et al. 2013) and can moderate the effect of treatment (Le Grange et al. 2012). The traits are an important component of a cognitive interpersonal model, which has been developed to explain the onset and maintenance of AN (Treasure and Schmidt, 2013). In this model cognitive features (obsessive compulsive and perfectionistic traits) are considered to increase the vulnerability to develop AN, and also contribute to the maintenance of the disorder through fostering pro anorexia nervosa beliefs and behaviours. One of the predictions from this model is that obsessive compulsive and perfectionistic traits are intermediate phenotypes, which arise from cognitive processing styles such as inflexibility and weak central coherence (WCC).

WCC refers to a cognitive style whereby there is a processing bias towards detail or local information at the expense of global integration or "gist" (both superior detail processing and poor holistic processing, Happé and Booth, 2008). A systematic review of the literature (Lopez et al. 2008) found consistent evidence of difficulties with global integration, however a bias towards superior local processing was not evident and therefore WCC in ED could not be confirmed. Since the previous review there have been

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further attempts to test the hypothesis of WCC in individuals with eating disorders. Several studies have shown a moderate to large superiority in detail processing tasks in the state of illness (Lopez et al. 2008; Tenconi et al. 2010) and after recovery (Lopez et al. 2009; Tenconi et al. 2010; Harrison et al. 2011; Roberts et al. 2012). Superior detail processing is also found in first-degree unaffected relatives (sisters) (Tenconi et al. 2010; Roberts et al. 2012; Kanakam et al. 2013). This suggests that a processing bias towards detail might be an inherited vulnerability of AN. Global integration is poor in acute AN, and it may be a consequence of low weight (Harrison et al. 2011).

The present study aims to provide an updated review and meta-analysis where possible of the current literature in order to test the hypothesis that individuals with ED display WCC. We hypothesise that those with AN will show strengths in detail/local processing and weaknesses in global integration.

Methods

The systematic review and meta-analysis was conducted according to the "PRISMA" statement (preferred reporting items for systematic review and meta-analysis, Moher 2009).

Eligibility criteria

Three authors conducted the search (KL, CL and KT) and studies were selected based on the following criteria:

1. Studies were published in English in peer-reviewed journals.
2. Studies employed the use of a neuropsychological measure of central coherence.
3. Studies contained participants with an ED and a healthy control (HC) comparison group.
4. Means, standard deviations and effect sizes were reported.
5. Minimum of 10 participants per group.

Information sources and search

Electronic databases were used to identify relevant articles. The databases used were Medline, Embase, PsychINFO, ISI Web of Science and Scopus. Searches were conducted between September 2008 and January 2014.

The same search strategy that was used by earlier systematic review by Lopez et al. (2008). The terms included in the first search were central coherence, cognition, information processing, neuropsychology, cognitive function, cognitive styles, local/global processing, field dependency/independence, holistic/analytic style, and abstract thinking. Following this the search was then narrowed down by searching for articles including ED populations (using the search terms anorexia nervosa, bulimia nervosa, eating disorders, binge eating disorder or bulimic disorder), in addition a search for tests and tasks used to measure central coherence (Rey-Osterrieth Figure Test, Group Embedded Figures Test, Object Assembly, the Fragmented Pictures Task, Matching Familiar Figures, overlapping figures test, Sentence Completion Task, Homographic Reading Test, Block Design) was also made. Reference lists of retrieved manuscripts were also manually searched for relevant studies.

Selection

Articles sourced from the initial search were then screened by the content of their abstracts, and then relevant manuscripts were retrieved. Full text articles were then assessed further for suitability (see Figure 1 for consort diagram of study selection).

Summary of measures

Five neuropsychological measures were used in studies that met the criteria for inclusion since September 2008. The tasks are listed in order of their popularity for studying central coherence in ED and their impact in the field.

Group/Embedded Figures Test (EFT/GEFT; Witkin et al. 1971/2002)

Participants are required to locate a simple shape within a much more detailed and complex shape. The time taken to find the embedded shape is recorded. Shorter times are indicative of detail-focused processing. As highlighted by Lopez et al. (2008) there are differences in the mode of administration of this task between studies, which contributed to a large variation in outcomes. When Happé et al. (2001) originally used this task to test the WCC hypothesis – both the object and the figure were presented simultaneously which minimized the working memory requirements. In the present study only studies using the non-memory version of the task (G/EFT) were included.

Rey-Osterrieth Complex Figure Test (ROFT; Osterrieth 1944)

A pen and paper task, in which participants copy a complex figure as accurately as they can. The

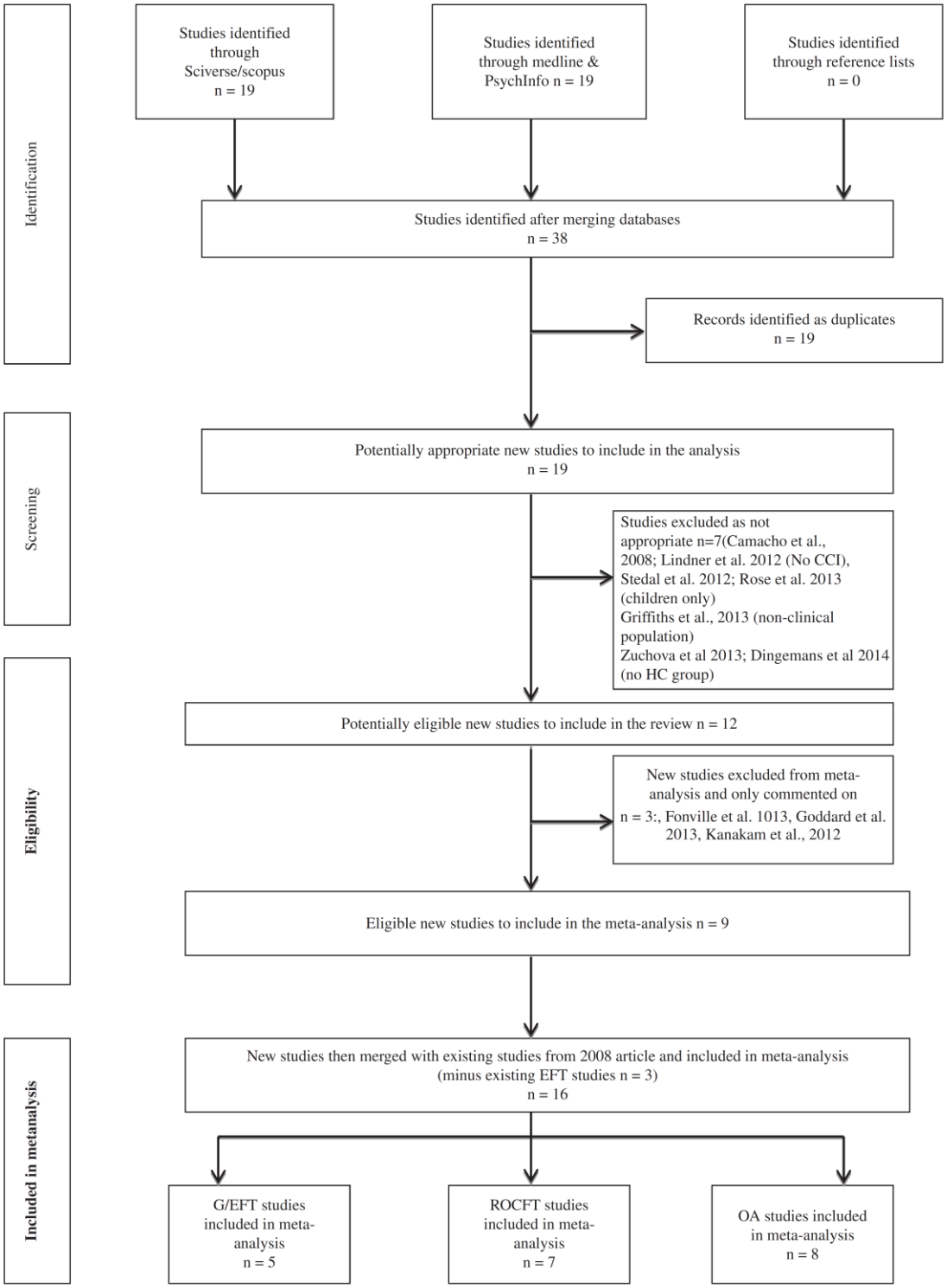


Figure 1. Flow diagram of study according to "PRISMA".

drawing style adopted by the individual is used to measure central coherence abilities. The central coherence index (CCI) is obtained from calculating the style index and the order index as defined by Happé's group (see Booth 2006 and Lopez et al. 2008b for references). A higher CCI score indicates a more global processing strategy. Only studies reporting the CCI as an outcome measure were included in the meta-analysis.

Object Assembly (OA, Wechsler 1974, 1981)

Participants are required to complete five jigsaw puzzles depicting familiar objects. The main outcome measure is the time taken to complete each puzzle. Time is scaled whereby higher scores (shorter times) indicate better global integration.

Overlapping Figures Test (OFT, Della Salla et al. 1995)

Participants are presented with a line drawing of a number of entangled objects. They must discriminate as many objects as they can in 4 min. Detecting a smaller number of objects indicates that the participant is more susceptible to distraction by the background details, and therefore is a marker of excessive local processing or weak global processing. Therefore performance on this task is benefited by global processing whereby better global integration will result in a higher score being obtained.

The Fragmented Pictures Task (FPT; Snodgrass and Vanderwart, 1980)

Participants are presented with a picture that forms slowly frame-by-frame over eight frames on a computer screen. Participants are instructed to respond verbally with what they think the picture is as soon as they know. If they guess incorrectly they may have another go. The outcome measure is the mean frame number. Slower responses (higher mean frame) are indicative of difficulties in global processing.

Synthesis of data

Means and standard deviations for ED participants and HC comparison groups were collated.

The mean difference in outcome measures between the AN and HC groups was standardised by calculating Cohen's *d*, the difference between the two raw means divided by the pooled standard deviation (Everitt 2003). A positive effect size means that the HC group performed better than the AN group. The standard error of each study's standardised effect size was calculated from the estimated effect and the group sizes of the two groups (Cooper and Hedges, 2009).

It was possible to conduct a meta-analysis for three tasks (GEFT, ROCFT and OA) by pooling the standardised effect sizes using a random-effects model. This model assumes that as well as within-group variability of scores (due to sampling error), variability of mean effect sizes is also caused by differences of the effect between studies (between-study heterogeneity). Random-effects models incorporate the between group heterogeneity. They result in estimates with wider confidence intervals than fixed-effects models, but are thought to be more realistic in psychiatric studies due to the variety of case mix and settings between studies (Everitt 2003).

Some studies reported several experimental groups (for example an anorexia nervosa group and a bulimia nervosa group) and compared them to only one control group. To avoid counting the control patients twice we followed the recommendation of the Cochrane Collaboration and divided the control group equally into two (or more groups) with smaller sample sizes, so that the total numbers of participants add up to the original size of the group.

Homogeneity between the studies was assessed using Cochran's Q-test and by calculating the measure of heterogeneity or inconsistency I^2 (Higgins et al. 2003). I^2 describes the percentage of total variation across studies that is due to heterogeneity rather than sampling error and ranges between 0% (no inconsistency) and 100% (high heterogeneity) with values of 25, 50 and 75% suggested as low, moderate, and high heterogeneity (Higgins et al. 2003).

Analyses were carried out in STATA 11 (StataCorp, College Station, TX, USA) using the user-contributed *metan* command for meta-analyses (Bradburn et al. 1998) and *metabias* (Steichen et al. 1998). Forest plots are used to graphically show the meta-analysis results.

Publication bias

Statistically significant results are more likely to be published than studies with non-significant results. The presence of publication bias on the results was assessed informally by visual inspections of funnel plots [a plot of a study's standard error or precision (1/standard error) against effect size]) using the user-written function metafunnel (Sterne 2003). If no publication bias is present the effect sizes should scatter randomly above and below true population effect size and the scatter gets wider as

the standard error (and sample size) decreases. Most studies should lie within the pseudo 95% confidence limits.

We also used Duval and Tweedie's (2000) non-parametric "trim and fill" method of accounting for publication bias in meta-analysis as implemented in STATA's user-written command *metatrim* (Thomas and Steichen, 2001). The trim and fill method imputes values estimated to be missing from the analysis due to for example publication bias, and re-estimates the effect size. If the conclusion of the meta-analysis remains unchanged following adjustment for the publication bias using the trim and fill method, the results can be considered as robust, excluding publication bias. Publication bias was only assessed if at least six studies were available. However, because the number of studies was small, any assessment of publication bias needs to be treated with caution.

Results

Study selection

A total of 12 new studies were identified from the search terms that were appropriate for inclusion in the review. It was possible to conduct meta-analyses on nine of the 12 studies, the remaining four studies were commented on individually. The meta-analysis also combined data from Lopez et al.'s (2008) review on studies utilizing OA, REY, and G/EFT (a total of seven studies). Therefore meta-analyses were performed on 16 studies in total.

One new study employed Block Design (BD; Van Autreve et al. 2013), however, the decision was taken to exclude BD from the present review due to concerns about the validity of this test as a measure of central coherence raised in the previous review (see Lopez et al. 2008).

A number of other neuropsychological tasks were also used since 2007 (The Overlapping Figures Test, OLFT; Fragmented Pictures Task, FPT); however, there were not enough studies to perform meta-analysis (OLFT $N = 1$, FPT $N = 1$), so these are commented on individually.

Study characteristics

A summary of all study characteristics can be found in Table I.

Fifteen studies included an anorexia nervosa group and a healthy control group. Five studies also included a bulimia nervosa group, six included a recovered ED or anorexia group, one included a mixed ED group and one mixed ED males.

Synthesis of results

The updated review includes data from G/EFT, FPT, OFT, OA, ROCFT. Meta-analysis are summarized below for those tests that were utilized in five or more studies (e.g., G/EFT, OA and ROCFT).

There were no new studies utilizing the Matching Familiar Figures Task, Sentence Completion Task and Homographic Reading Task since the 2008 review.

The results are presented in order of the tasks popularity for studying central coherence in ED and the impact they are currently having in the ED field.

Group/Embedded Figures Task (G/EFT)

The G/EFT was used in four new studies since 2008. However, three studies were excluded from the meta-analysis (Fonville et al. 2013; Goddard et al. 2013; Kanakam et al., 2013). Fonville et al. (2013) was excluded from the analysis as they used a modified version of the EFT for fMRI study, in which participants were asked to indicate in which of two shapes the embedded figure appeared. Goddard et al. (2013) was excluded due to the sample only including males. Kanakam et al.'s (2013) sample consisted largely of individuals recovered from an ED, and so was excluded.

Meta-analyses were performed only on data where the working memory component had been excluded.

A random effects meta-analysis of $N = 5$ studies (Figure 2) including only AN groups showed a pooled effect size of $d = -0.63$ (95% CI = −0.87, −0.39, $P = <0.001$). Four studies also included a BN group. There was a pooled effect size of $d = -0.28$ (95% CI = −0.58, 0.03, $P = 0.08$). Three studies report EDREC data. A random effect meta-analysis showed a pooled effect size of $d = -0.62$ (95% CI = −0.94, −0.31), $P < 0.001$. When data from all ED subtypes was pooled there was an effect size of $d = -0.51$ (95% CI = −0.67, −0.35), $P = 0.0025$).

There was little heterogeneity across the studies ($x^2(11) = 11.35$, $P = 0.41$, $I^2 = 3.1\%$) or within the sub-studies (AN: $I^2 = 0\%$. $P = 0.79$, BN: $I^2 = 20.4\%$. $P = 0.29$ and REC: $I^2 = 0\%$, $P = 0.44$).

Publication bias

A funnel plot using studies of all ED sub-types suggested some minor asymmetry. There were more studies with larger negative effect sizes (Figure 3). However, the trim and fill method did not estimate any missing studies.

Table I. Study demographics.

Author/Date	Group	*N*	Age	BMI	IQ	Medication	Comorbidities
Thompson et al. (1993)	AN	10	25.8	>15% normal weight	115.8	N.R	40%dep; ++ OCD
	HC	10	23.2		119.7	N.R	None
Gillberg et al. (1996)	AN	51	21	21.2 (3.5)	102.9	N.R	10 ASD
	HC	51	20.8	21.2 (2.3)	106.5	N.R	None
Mathias and Kent et al. (1996)	AN	34	22.7 (7.4)	15.3 (1.7)	96.1 (8.8)*	33%	++ anxiety; ++ dep
	HC	31	20.8 (2.4)	22.8 (2.4)	101.1 (6.9)*	None	None
Galderisi et al. (2003)	AN	14	23.7 (4.54)**	15.3 (2.23)	100 (10.8)**	None	None
	BN	31	23.7 (4.54)	21.5 (2.30)	100 (10.8)	None	4 dep; 4PD
	HC	45	24.2 (4.8)	N.R	101.1 (13.6)	None	None
Tokley and Kemps et al. (2007)	AN	24	21.9 (5.3)	16.8 (1.5)	Matched	N.R	++ OCD; ++ anxiety; ++dep
	HC	24	22.0 (5.0)	22.7 (4.3)		N.R	None
Gillberg et al. (2007)	AN	47	24.5	22.2 (4.1)	105.2*	N.R	N.R
	HC	51	24.2	22.2 (3.4)	109.4	N.R	N.R
Lopez et al. (2008b)	AN	42	28.4 (9.6)	15.8 (1.7)	112.8 (6.8)	40.5%	++OCD; ++Anxiety; ++Dep
	BN	42	27.0 (7.2)	21.7 (2.4)	111.8 (6.9)	16.7%	++OCD; ++anxiety; ++dep
	HC	42	26.3 (6.4)	21.9 (2.7)	112.2 (5.4)	None	None
Lopez et al. (2009)	EDREC	42	25 (21-31)	20.9 (2.2)	113.6 (5.3)	None	+OCD, +Anxiety, +Dep
	HC	42	26.3 (6.4)	21.9 (2.7)	112.2 (5.4)	None	None
Tenconi et al. (2010)	AN	60	26.2 (6.9)	16.2 (1.5)	N.R	N.R	N.R
	EDREC	63	N.R	20.5 (3.1)	N.R	N.R	N.R
	HC	120	27.4 (4.5)	21.8 (3.0)	N.R	N.R	N.R
Harrison et al. (2011)	AN	50	N.R	N.R	111.40 (8.64)	N.R	N.R
	BN	48	N.R	N.R	109.65 (6.95)	N.R	N.R
	ANrec	35	N.R	N.R	109.12 (8.12)	N.R	N.R
	HC	89	N.R	N.R	112.27 (7.39)	N.R	N.R
Kim et al. (2011)	AN	22	22 (6.96)	15.63 (1.47)*	105.17 (9.14)	N.R	N.R
	BN	28	23.04 (4.57)	20.40 (2.72)*	110.88 (12.23)	N.R	N.R
	HC	26	23.46 (4.14)	21.36 (2.78)	113.04 (10.52)	N.R	N.R
Roberts et al. (2012)	ANR	35	23.71 (6.39)	17.98 (2.18)	N.R	N.R	N.R
	ANBP	33	25.58 (7.64)	17.88 (3.00)	N.R	N.R	N.R
	BN	30	26.43 (6.84)	21.66 (2.94)	N.R	N.R	N.R
	ANrec	30	32.13 (11.64)	20.76 (1.75)	N.R	N.R	N.R
	HC	88	28.43 (8.47)	22.07 (1.79)	N.R	N.R	N.R
Danner et al. (2012)	AN	16	25.63 (5.41)	14.65 (1.70)	N.R	N.R	N.R
	ANrec	15	24.33 (4.72)	21.20 (1.82)	N.R	N.R	N.R
	HC	15	25.80 (4.69)	21.46 (2.29)	N.R	N.R	N.R
Kanakam et al. (2013)	MZ ED	26	31 (25)	20.6 (3.30	108 (14)	N.R	N.R
	DZ ED	10	35 (24.75)	21.15 (2.25)	111.5 (14)	N.R	N.R
	MZ HC	17	54 (32)	21.9 (7)	110.5 (15.5)	N.R	N.R
	DZ HC	4	52 (34.50)	23.65 (4.3)	113 (14.8)	N.R	N.R

(Continued)

Table I. Continued.

Author/Date	Group	*N*	Age	BMI	IQ	Medication	Comorbidities
Fonville et al. (2013)	AN	35	23 (9)	16.0 (1.6)	110 (9)	46% SSRI	N.R
	HC	37	25 (4)	21.9 (1.9)	117 (10)	0%	N.R
Van Autreve et al. (2013)	AN	51	26 (12)	14.4 (2)	N.R	N.R	++OCD; ++Dep;
	HC	26	19 (2)	20.9 (1.8)	N.R		
de Sampaio et al. (2013)	AN	24	24.5 (7.6)	18.1 (1.8)	102.5 (19.8)	54.2% psychoactive	+Anx; +Dep
	BN	24	24.4 (6)	25 (6.5)	96.5 (16.0)	62.5% psychoactive	+Anx; +Dep
	HC	24	25.2 (6.9)	21.5 (18.1)	100.2 (15.2)	0%	
Goddard et al. (2013)	Mixed ED (males)	29	26.2 (8.2)	17.2 (2.2)	106.9 (9.4)	N.R	N.R
	HC (males)	42	26.4 (7.2)	23.2 (2.5)	108.4 (8.2)	N.R	N.R

BMI, Body mass index; AN, anorexia nervosa; BN, bulimia nervosa; ED, eating disorder; ANrec, recovered anorexia nervosa; HC, healthy control; MZ, mono zygotic, DZ, dizygotic; dep, depression; OCD, obsessive compulsive disorder; ASD, autistic spectrum disorder; SA, substance abuse; GAD, generalized anxiety disorder; PD, personality disorder. *Significant differences between groups. **The authors reported age and IQ grouping AN and BN.

Fonville et al. (2013) reported no differences between AN and HC groups in terms of reaction times. Goddard et al. (2013) reported that ED males were slower at detecting the complex shapes than HC males ($d = -0.6$, $P = 0.022$). Kanakam et al. (2013) reported no differences between ED twins and HC twins ($d = 0$, $P = 0.98$).

Rey-Osterrieth Complex Figures Test (ROCFT)

The ROCFT was employed by seven studies, which fulfilled the inclusion criteria with ED populations. Three studies were excluded. Goddard et al. (2013), as it included only a male ED population, Kanakam et al. (2013) as its sample mainly consisted of recovered ED participants. Goddard et al. (2013), found that ED males had weaker central coherence than HC males ($d = -0.5$, $P = 0.009$). Kanakam et al. (2013) reported no differences between ED twins and HC ($d = 0.1$, $P = 0.054$).

Seven studies employed ROCFT with an AN population. A random effects meta-analysis showed a pooled effect size for CCI of $d = -0.63$ (95% CI $= -0.85$, 0.42), $P < 0.001$. Four studies report data from a BN population. A random effects meta-analysis showed a pooled effect size for CCI of $d = -0.84$ (95% CI $= -1.16$, -0.52), $P < 0.001$. Lastly, five studies reported data comparing participants recovered from an ED (mixed). A random effects meta-analysis demonstrated a pooled effect size for CCI of $d = -0.49$ (95% CI $= -0.71$, -0.26) $P < 0.001$ (Figure 4). When data from all ED studies was pooled there was an effect size of $d = -0.63$ (95% CI $= -0.77$, -0.49, $P < 0.001$).

There was evidence of heterogeneity across the studies combined ($x^2(13) = 7{,}55$, $P = 0.297$, $I^2 = 13.6\%$), including those with AN ($P = 0.321$, $I^2 = 14.3\%$) and BN ($P = 0.304$, $I^2 = 17.3\%$).

Publication bias

An assessment of funnel plots did not indicate any publication bias and the trim and fill method did not estimate any missing studies using all or AN studies only (Figure 5).

Object assembly (OA)

Figure 6 presents all eight studies employing OA with ED populations in a meta-analysis. Since 2008, only one study employed OA with an ED population (Tenconi et al. 2010). Eight studies used OA with an AN population. Lower scores, indicating poorer global integration were observed in AN participants in all but one study (Galderisi et al. 2003). A random effects meta-analysis showed a pooled

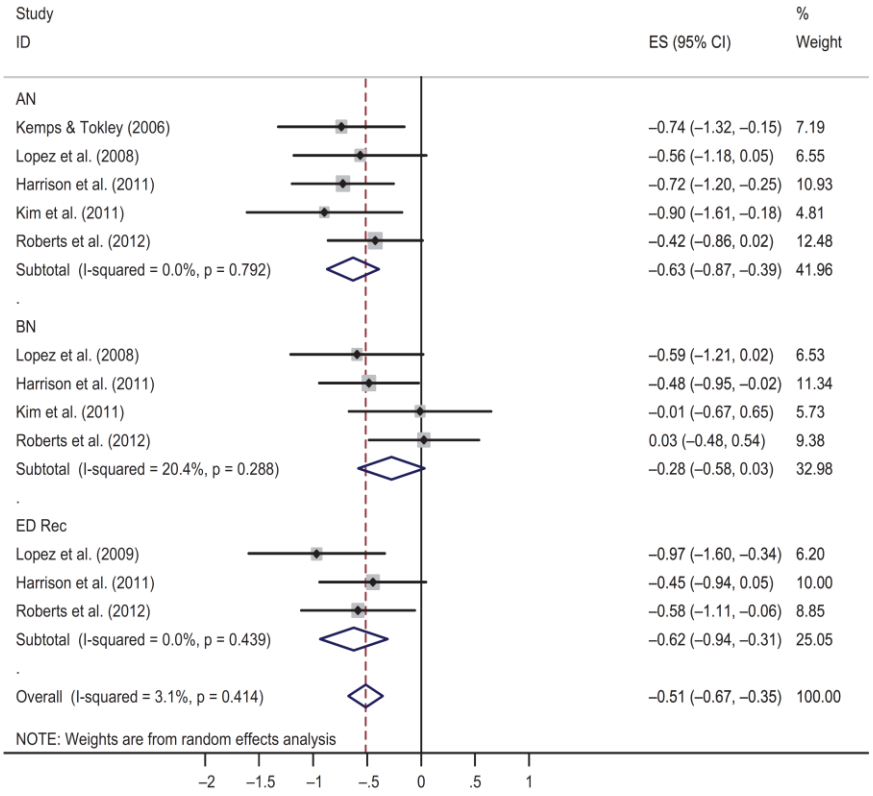


Figure 2. Forest plot for G/EFT studies.

effect size of $d = -0.58$ (95% CI = −0.86 to −0.29), $P < 0.0001$.

One study also recruited a BN group (Galderisi et al. 2003), which (in contrast to their AN group) showed a lower score compared to HCs [$d = -0.44$ (95% CI = −0.91, 0.02, $P = 0.063$)]. One study observed OA performance in recovered AN (Tenconi et al. 2010), also showing lower scores and therefore poorer global processing compared to HCs [$d = -1.48$ (95% CI = −2.01, −0.95), $P < 0.001$]. For all subtypes there was a pooled effect size of $d = -0.65$ (95% CI = −0.94, −0.37, $P < 0.0001$.

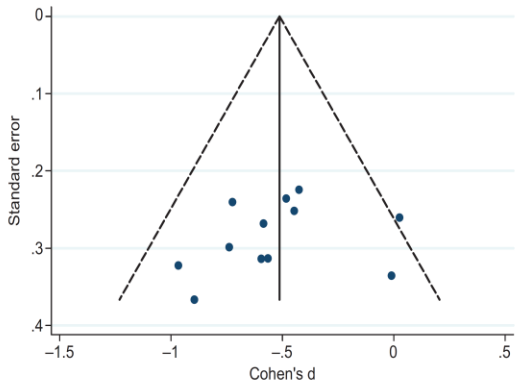


Figure 3. Funnel plot of Group/Embedded Figures Test (G/EFT) studies.

There was evidence of moderate heterogeneity across all studies ($x^2(9) = 27.35$, $P = 0.001$, $I^2 = 67.1\%$) including those with AN only ($x^2(7) = 16.41$, $P = 0.022$, $I^2 = 57.3\%$).

Publication bias

An assessment of the funnel plot did not indicate any publication bias using AN groups or all ED subtypes (Figure 7) The trim and fill method estimated that there were no missing studies.

Overlapping Figures Test (OFT)

Tenconi et al. (2010) used the OFT and found that fewer shapes were detected by the AN group compared to HCs ($d = -0.61$) meaning that those with current AN showed excessive local processing and weak global processing. The same paper also reported data from a recovered group, who also detected fewer shapes than HCs ($d = -0.61$).

Fragmented Pictures Task (FPT)

Harrison et al. (2011) used the FPT. They found that the ED group (including AN, BN and REC) took significantly longer to discern what the picture was compared to the HC group ($d = -0.82$). This effect

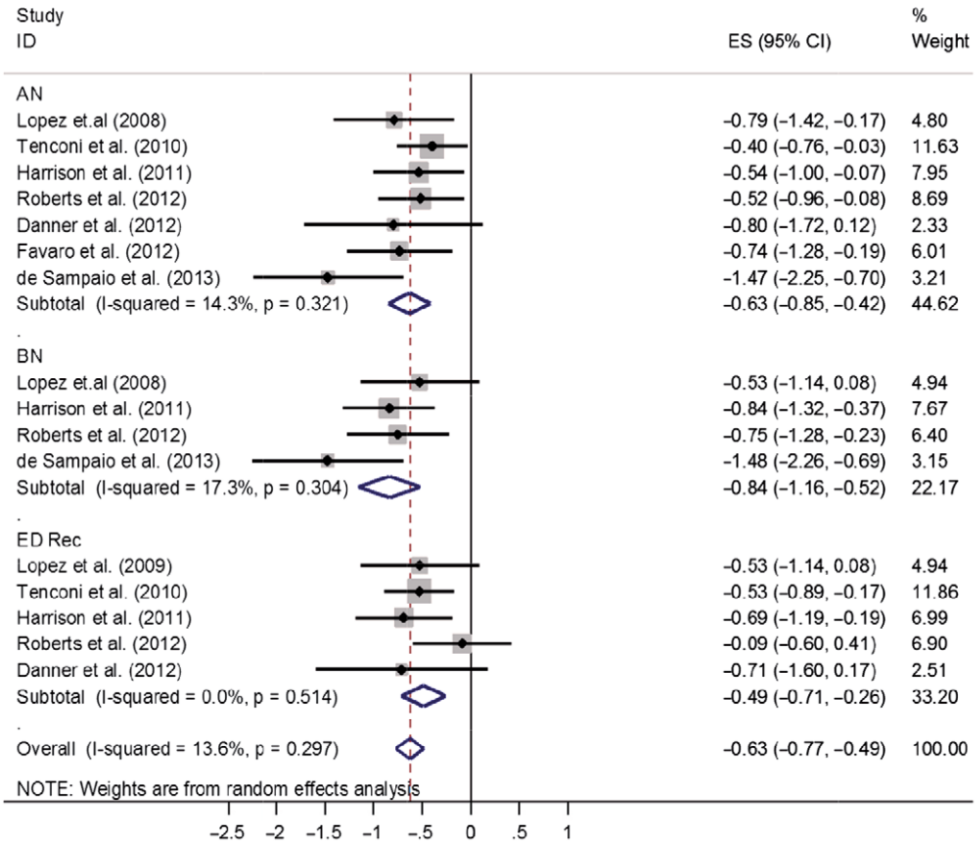
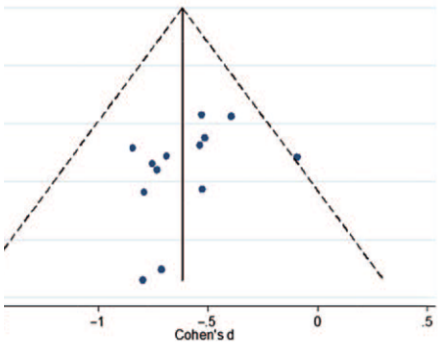


Figure 4. Forest plot of Rey Osterrieth Complex Figures Test (ROCFT).

the AN group versus the HCs ($d = -0.81$). ce no differences in performance between ecovered group and HCs. Goddard et al. ed the FPT with a male ED population eported that compared to HC comparison y too had difficulty with global integration , $P = 0.022$).

on

of the present study was to provide an systematic review and meta-analysis in



nnel plot of Rey Osterrieth Complex Figures Test udies.

order to test the hypothesis that individuals with ED display Weak Central Coherence (WCC). The results confirmed the hypothesis, with individuals with ED displaying a bias towards detail at the expense of global integration.

The present review found new studies using the G/EFT to examine local processing, and new studies using the ROCFT, OA, OFT and FPT to examine global processing.

The strongest evidence of extreme local processing came from the G/EFT. A bias towards details over the global "gist" was consistently demonstrated in all studies using this measure, and this finding was robust across ED subtypes with medium effect sizes (−0.51), particularly in AN. Evidence of inefficient global processing was also demonstrated, with the ROCFT being the most popular measure of global processing. Poorer performance on the ROCFT was evident across all ED subtypes with medium effect sizes (−0.62). Further evidence of inefficient global processing across ED subtypes was also found in studies using the OA, OFT and FPT (medium-large effect sizes).

This review therefore provides the first strong evidence of a bias towards detail-focused processing in ED, along with further consistent evidence of suboptimal global processing on numerous tasks.

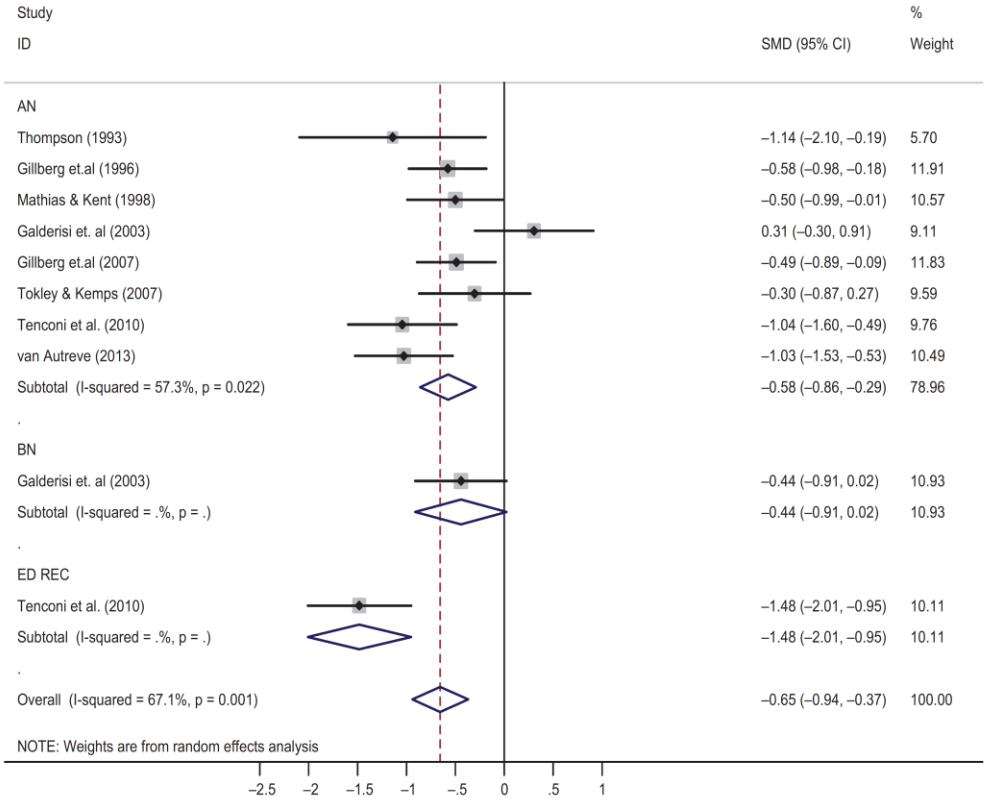


Figure 6. Forest plot of Object Assembly (OA) Studies.

Taken together, these results give evidence of WCC in this population.

As with the previous review (Lopez et al. 2008), there was little variation in the size of the effect between the diagnostic sub-groups of eating disorders. A bias towards detail over global integration was observed on a number of tasks across the spectrum of ED, with this profile being most accentuated amongst those with AN. Currently there are fewer studies examining WCC in those recovered from AN, however the existing literature demonstrated that recovered individuals exhibited an intermediate profile, whereby their performance was in between those with AN and healthy control counterparts. The observation that this information processing bias continued to be present in both the acute or recovered stage of illness (albeit it on a continuum) provides some support for the notion that Weak Central Coherence (WCC) may be an endophenotype for ED. However, further studies utilising recovered individuals, siblings and family members are needed to provide stronger support to this hypothesis.

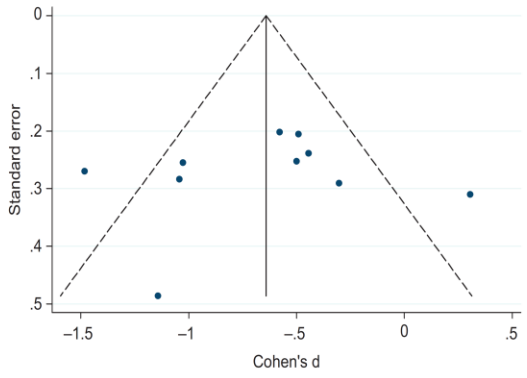


Figure 7. Funnel plot of Object Assembly (OA) studies.

These findings have important clinical implications. Conventional psychological treatments are not associated with good outcomes for many individuals with ED. Elucidating potential predisposing and maintaining factors for the disorder may lead to more effective tailor-made treatments and consequently improve treatment outcome. Underlying cognitive traits such as WCC may interact with, and exaggerate perfectionistic and obsessive-compulsive personality traits, which may make engaging in psychological treatments that emphasise behavioural change difficult. Future treatments may focus first on targeting core cognitive characteristics such as WCC, prior to attempting to create behavioural change. For example, Cognitive Remediation Therapy (CRT) has been developed to target maintaining factors, by encouraging "bigger picture" and flexible thinking (Tchanturia et al. 2013a). A case series using CRT showed improvements with medium

effect sizes in CC index after 10 sessions of CRT (Tchanturia et al. 2008). As CRT is associated with cognitive improvements, it could therefore prepare individuals for engagement in treatment that then directly target ED pathology.

The finding that WCC is a transdiagnostic trait in ED also carries important clinical implications. There is a wealth of research supporting inefficient cognitive processing in AN, however, its presence in individuals with BN is a fairly novel finding. Although it is the first line recommended treatment for BN, Cognitive Behaviour Therapy (CBT) is not effective for approximately 35% of patients (Agras et al. 2000; Fairburn et al. 2003; Shapiro et al. 2007). The treatment refractoriness of such patients could be due to the cognitive style they are exhibiting, and information regarding their cognitive profile could be used to help make slight treatment modifications to traditional CBT to increase engagement and ultimately improve outcomes.

A preference for detailed processing over global integration is not specific to ED and has been observed across a number of disorders, for example in both Obsessive Compulsive Disorder (OCD; Kuelz et al. 2004) and Autistic Spectrum Condition (ASC; Booth 2006).

Such disorders exhibit similarities in cognitive styles across a number of domains including WCC and set-shifting/cognitive rigidity. More recently there have also been parallels drawn between the socio-emotional profile of AN and ASD (Tchanturia et al. 2013b). Along with this, there are also inflated comorbidity rates of both OCD and autistic traits within AN samples (Swinbourne et al. 2007; Tchanturia et al. 2013b). These elevated comorbidity rates, along with shared neuropsychological traits and clinical symptomatology, strongly hint that these disorders share a common underlying mechanism. Such thinking further highlights the importance of tailoring treatments for ED populations, for example incorporating work focusing on neurocognition and emotion skills training (Davies et al. 2012), to target both obsessive-compulsive and socio-emotional symptoms.

This study has some limitations in that tasks such as the ROCFT do not only measure global or local processing, but instead examine the tradeoff between the two.

Following on from this, many neuropsychological tasks not only measure one element of cognition, but instead measure an array of cognitive functions. For example the ROCFT can be used to examine numerous abilities such as memory, planning, organization, as well as central coherence. It is therefore impossible to isolate the particular property one intends to study. The authors have assumed this potential bias in the interpretation of the results and conclusions are supported with a careful examination of several tasks aimed to explore the same concept.

Secondly, many studies do not describe their exact method of administration or comment on comorbidities or medication, therefore leaving the effect of possible biases unknown. With this in mind, it is also important to highlight some inconsistencies within the Object Assembly results. One study (Galderisi et al. 2003) found the opposite result to the other seven studies (finding that the AN group performed more globally than the HC). Such inconsistencies could be attributed to differences in methodologies, and further inspection highlighted that this study had recruited drug-naïve AN patients (where as a majority of other participants had been medicated), and this may have therefore had an effect on neuropsychological performance.

In conclusion, this study has provided evidence supporting the WCC hypothesis in ED transdiagnostically. As well as adding to the existing evidence for inefficient global processing in this group, it has also provided further evidence of superior local processing. The persistence of WCC following recovery also provides partial support to the endophenotype hypothesis for ED.

Statement of Interest

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Since the publication of this study there have been no published studies examining central coherence in adults with AN.

1.8.5 Central coherence in unaffected AN relatives

Only one published study has investigated central coherence in unaffected relatives of those with AN. Roberts, Tchanturia, and Treasure (2013) found lower levels of global processing on the ROCFT in unaffected sisters compared to HC sisters. Additionally, the unaffected sisters group also demonstrated superior detail-focused processing on the Group Embedded Figure Test (GEFT, (Witkin, 1971), suggesting that unaffected sisters of those with AN also possess WCC (Roberts et al., 2013).

1.8.6 Central coherence in children and adolescents with AN

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A Systematic Review of Central Coherence in Young People with Anorexia Nervosa

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Abstract

Objectives: It is hypothesised that Weak Central Coherence (superior attention to detail with poorer bigger picture thinking) is a possible endophenotype for Anorexia Nervosa (AN). Currently the neuropsychological profile of children and adolescents with AN in unclear. The present review aimed to summarise the available literature with regards to the central coherence abilities of children and adolescents with AN, and clarify their neuropsychological profile.

Method: The search found seven eligible studies. Meta-analyses were not possible due the variation in tasks used.

Results: Evidence of less efficient global processing in children with AN was observed in a number of studies. The strongest evidence was observed from studies using the Rey Osterrieth Complex Figures Test (ROCFT). A visual comparison of ROCFT from child and adult AN studies highlighted similarities in global processing profiles.

Conclusions: Evidence of inefficient global processing was observed across a number of studies. However methodological flaws in the current literature were highlighted and made interpretation difficult. These are discussed and recommendations for future research are made.

Keywords: Anorexia nervosa; Central coherence; Global processing; Children; Adolescents; Systematic review.

Introduction

Anorexia Nervosa (AN) is an eating disorder characterised by persistent restriction of calorie intake, a fear of gaining weight and a disturbance in body perception [1]. With limited effective treatment options for AN, research interests within the eating disorders field have recently turned to examining possible underlying factors and traits such as cognitive processing styles. This work has highlighted that adults with AN exhibit a specific neuropsychological profile with certain areas of weakness (relative to their IQ), that may help to maintain the disorder, namely that of inefficient set-shifting [2-4] and weak central coherence [5]. Weak central coherence refers to a cognitive processing style whereby there is a relative lack of gistful 'bigger picture' thinking alongside superior attention to detail [6]. This evidence along with observations of similar profiles in those recovered from AN and also in unaffected relatives [7,8] has led to the postulation that rather than being a consequence of long-term starvation, they are in fact representative of endophenotypes for AN. An endophenotype is a measurable component in between a genotype and a phenotype for a disorder. It must be heritable and persist regardless of illness status [9]. What is lacking from the literature, and needed to provide further support for the endophenotype hypothesis, is clarity regarding the neuropsychological profile of children with AN. Studying neuropsychological processing in younger populations with AN is beneficial as we would expect any neurological scars as a consequence of starvation to be minimal, and therefore any underlying premorbid traits should be more prominent.

A recent systematic review and meta-analysis aimed to clarify set shifting abilities of children and adolescents with AN [10]. Overall this review found no significant differences between children with and without AN. It is important to note that this work is in its early stages and data is limited, therefore these results should be interpreted with caution. To our knowledge there are no published systematic reviews of the literature with regards to central coherence abilities in children and adolescents with AN, and such information would be beneficial to the field both in a research and clinical sense. Therefore the aim of the present study is to review the available literature examining central coherence abilities in children and adolescents with AN, in order to help clarify the neuropsychological profile of this group.

Method

The systematic review was conducted according to the 'PRISMA' statement (preferred reporting items for systematic review and meta-analysis, [11]. Figure one shows the consort diagram for the study selection.

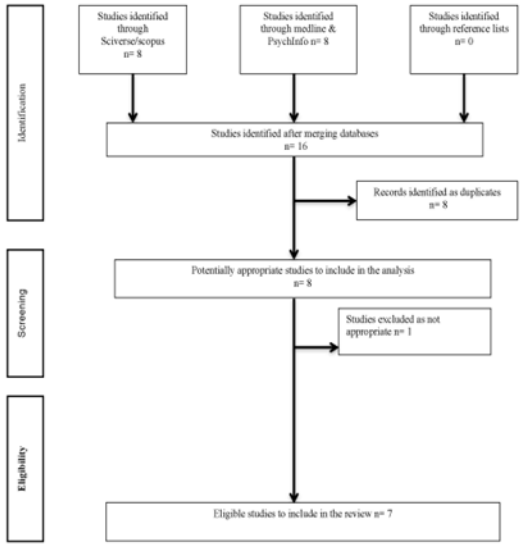

Figure 1: Flow diagram of study according to 'PRISMA'

Eligibility criteria

Both authors conducted the search and studies were selected based on the following criteria:

1. Studies contained adolescents with a diagnosis of AN.
2. Studies employed the use of a neuropsychological measure of central coherence.
3. Means and standard deviations were reported.

Information sources and search

Electronic databases were used to identify relevant articles. The databases used were Medline, Embase, PsychINFO, ISI Web of Science and Scopus. Searches were conducted up until May 2014.

Selection

Articles sourced from the initial search were then screened by the content of their abstracts, and any relevant manuscripts were retrieved. Full text articles were then assessed further for suitability.

Summary of measures

The following neuropsychological measures were used to measure central coherence:

Rey-Osterrieth Complex Figure Test (ROFT, [12]).

The ROCFT is a pencil and paper task used to assess a number of executive functions such as memory, planning, organisation, as well as central coherence. When using the ROCFT to assess central coherence, performance is benefited by a global approach. Previously, this task was scored according to accuracy scores [13], whereby the participant is ask to copy directly from the picture and then again from memory after a delay. The delayed recall accuracy score has been used as an indirect measure of central coherence, as it was believed that the way the object is processed in the direct copy phase (either globally or fragmented) will have an effect on the ability to recall it later, with global strategy in the copy phase benefiting later recall.

More recently, when exploring cognitive profiles in Autism, Booth and colleagues developed a scoring system which is thought to tap into the concept of central coherence more accurately. A Central Coherence Index (CCI) is generated from calculating both an order and style index [14]. A higher CCI is indicative of more efficient global processing. This scoring system was effectively applied and explored within the eating disorder literature [3,8,15,16]. Six studies employing samples of adults with AN demonstrated that adults with AN performed significantly less globally than those without AN (d=-0.56 (95% C.I. -0.76, 0.35), p<0.001 [5].

Object Assembly (OA, [17]).

Participants are required to complete 5 jigsaw puzzles depicting familiar objects. The main outcome measure is the time taken to complete each puzzle. Time is scaled whereby higher scores (shorter times) indicate better global integration.

Overlapping Figures Test (OFT,[18])

Participants are presented with a line drawing of a number of entangled objects. They must discriminate as many objects as they can in 4 minutes. Detecting a smaller number of objects indicates that the participant is more susceptible to distraction by the background details and therefore is a marker of local processing.

Groton Maze Learning task (sub-test of the Cogstate Computerised test battery [19]).

Participants are required to navigate through a computerised maze. Navigation is aided by adopting a more global approach (e.g. thinking about the overall 'bigger picture' rather than focussing on small details such as the next move).

Synthesis of data

Means and standard deviations from the AN groups were collated along with the means and standard deviations of healthy control groups where available.

Results

Study selection

A total of eight studies were found from using the search terms. However one study was excluded from the review [20] as means and standard deviations were not reported. There was also one study [21] that had employed the use of block design, but since this was not recognised as a valid measure in the adult AN literature, the decision to exclude this study was made [15]. One study [22] that had used the Group Embedded Figures test [23], but as this study did not use a HC comparison group and there were no other child AN studies to informally compare the data to, the decision was taken to exclude this data from the review.

Study Characteristics

A summary of all study characteristics can be found in Table 1. Five of these studies employed an AN and HC group. However two studies did not include HC groups [22,24]. All participants in the AN groups met the DSM-IV criteria for Anorexia Nervosa, with the exception of [25] whose sample also included Bulimia Nervosa and Eating Disorders Not Otherwise Specified.

Author/ date	Group	N	Age (years)	Age range (years)	BMI	IQ
Tenconi et al., (2010)	AN	60	26.2 (6.9)	14-47	16.2 (1.5)	N.R
	HC	120	27.4 (4.5)	N.R	21.8 (3.0)	N.R
Andres-Perpina et al., (2011)	AN	37	15.4 (1.5)	N.R	Below 17.5	N.R
	HC	41	15.4 (1.5)	N.R	NR	N.R
Rose et al., (2011)	AN	9	14.9 (1.39)	12.4-16.08	16.41 (1.38)	N.R
Allen et al., (2012)	AN	58	17.5 (0.26)	15-18	24.78 (8.10)*	N.R
	HC	542	16.98 (0.24)	N.R	22.55 (5.09)	N.R
Frampton et al., (2012)	AN	15	19 (1.95)	9.7-21.2	88.13 % w4h (12.19)	113.27 (10.15)
	HC	15	18.3 (2.20)	13.11-21.7	106.39 % w4h (9.79)	114.37 (13.80)
Stedal et al., (2012)	AN	114	17.1 (3.2)	9.5-27.1	16.3 (2.0)	N.R
	HC	66	N.R	N.R		N.R
Dahlgren et al., (2013)	AN	20	15.9 (1.6)	13-18	16.81 (1.63)	N.R
						N.R

Notes: N=Number of participants, BMI=Body mass index (BMI; Kg/M2), N.R=Not reported

*This sample is inclusive of AN, BN and EDNOS participants** This study is separated into two cohorts in the meta-analysis based on brain function

Table 1: Study demographics

Synthesis of results

Rey-Osterrieth Complex Figure Test (ROFT; [12]). The ROCFT was used in 6 studies [21,22,24,26-28]. The methods for scoring the ROCFT varied between studies with the most consistently used method of scoring was Booth's (2006) where by the order and style indices are calculated and contribute to a central coherence index (CCI). This method was adopted by four studies [21,22,24,27,28], is presented as two separate studies, as the AN sample was divided into two subgroups. The subgroups (hypo-perfusion and normal-perfusion) were based on neurobiological status reflecting results from a brain scan that measured regional cerebral blood flow (rCBF). Two of these studies did not have a HC comparison group, therefore to utilise this data the means for all studies have been plotted in figure 2, to enable visual comparison between all studies.

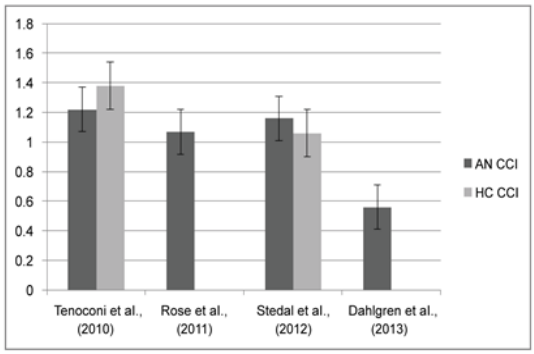

Figure 2: Means (standard errors) of studies reporting the CCI in children and adolescents with AN.

Stedal et al., (2012) found no significant differences on the ROCFT, with their reported raw means and standard deviations suggesting that the AN group performed more globally than the HCs (d=0.25, small effect). Tenconi et al., (2010) reported lower CCIs in the AN group compared to the HCs, suggesting less efficient global processing in the AN group (d=0.46). These results should be interpreted with caution as this sample was inclusive of children and adults (age range 14-47 years). Rose et al., [22] and Dahlgren et al., [23] did not utilise HC groups. Figure 2 compares their ED group performance with the HC data from the other studies, and suggests that both of the AN groups demonstrated lower CCIs and therefore less efficient global processing than the other studies HC groups. Four studies did not use Booth's [14], method to score the ROCFT, but instead reported the accuracy score for the delayed recall. Frampton et al., [28] reported significant differences between the hypoperfusion AN groups and the HC group in delayed visual recall of the ROCFT with AN group performing worse (p=0.001, d=2.35, huge effect). There were no differences in performance between the normal perfusion AN group and the HC group. Andres-Perpina et al., reported no significant differences in ROCFT recall score between AN and HCs (p=0.058, d=0.47, medium effect). Tenconi et al., also reported no significant differences in delayed recall scores between AN and HC (d=0.38).

Object Assembly (OA, [15]).

One study employed OA [21] and reported lower scores in the AN group, suggesting poorer global integration. However, these scores are inclusive of adult data as well as child.

'Overlapping Figures Test (OFT [16]).'

One study used the OFT, and reported that those with AN detected fewer shapes, suggesting that they were showing superior local processing. These results are inclusive of adult data.

Groton Maze Learning task (sub-test of the Cogstate Computerised test battery[17]).

One study (Allen et al.,) used the GMLT to assess global processing and found worse performance in the ED group compared to the HC group ($p=<0.05$).

The ROCFT: Comparison with the adult Anorexia Nervosa literature.

Figure 3 compares the CCI means from the child and adolescent AN literature with that of the adult AN literature.

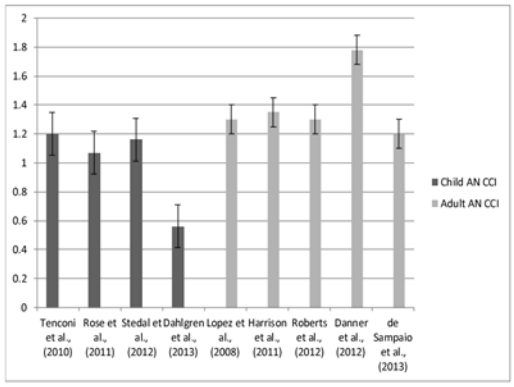

Figure 3: Mean (standard errors) CCI scores of child and adolescent AN studies and adult AN studies.

This visual comparison suggests that children and with AN are performing in a similar way to adults with AN with regards to the CCI, and demonstrating inefficient global processing on this task.

Discussion

This study aimed to systematically review the available literature assessing central coherence abilities in children and adolescents with anorexia nervosa. The review found a number of studies utilising neuropsychological measures of central coherence with children and adolescents with AN. A meta-analysis was not possible due to the large variation in tasks used between the studies.

The most popular neuropsychological measure was the ROCFT, with 'six' studies utilising it. There was some variation in the administration and scoring methods for this task, with four studies using Booth's [14], method to obtain a CCI. Overall the findings from these studies suggested that children and adolescents with AN had a lower CCI score, therefore indicating a less globally-orientated processing style then the HC groups. Several studies used the ROCFT delayed recall accuracy scores to assess central coherence. Overall these studies did not find any differences in accuracy scores between AN and HC groups, which led a majority of the authors to suggest that there were no differences in central coherence abilities. The validity of using this method a measure of central coherence will be discussed. There were a number of other measures used to assess central coherence with children. Overall, these studies showed poorer performance by the AN group on tasks that were benefited by a more global approach (the Overlapping figures task, and the Groton Maze Learning task). However, it is important to note that two of these studies also included data from adults with AN, and therefore such poor performance cannot be attributed to the younger AN population alone. This manuscript attempted to informally compare the ROCFT CCI scores from the child AN literature with those from the adult literature. When presented in a bar chart (Figure 3) the results suggested that the CCI scores of children with AN are similar to that found in adults with AN, suggesting an inefficient global processing style. However, such comparisons are very preliminary and further well powered, planned comparison studies are needed in order to confirm any differences and similarities in profiles. The present review highlighted a number of methodological limitations that made interpretation of the available data challenging. The large variation in the number of tasks used to assess central coherence meant that it was not possible to conduct a meta-analysis of the available data. As previously mentioned there was also variation found in the scoring methods of the same tasks, namely the ROCFT, whereby either studies had calculated a CCI or had used the delayed recall accuracy scores. Historically the accuracy scores from the delayed recall phase have been used as an indirect measure of detail focussed processing, as it was believed the way in which the shape is processed in the copy phase had a knock on effect on the ability to accurately recall the shape at a later stage. As differences were found between AN and HC groups when using the CCI but not with accuracy scores, this may suggest that delayed recall performance may not be a sensitive enough measure of central coherence abilities, as the accuracy in which the figure is drawn may not be a precise representation of global versus detail focussed processing. In comparison, the central coherence, style and order indices can give us more insight into the processing style, as they directly examine the order and style in which the participant attends to each feature, therefore providing a more sensitive measure of whether the participant is focussing on smaller featural details or larger global elements.

The CCI is therefore a more accurate and direct measure of central coherence abilities, and for this reason it would prove beneficial to use it more consistently. It is also the most widely used scoring method within the adult AN literature, and therefore using the CCI more consistently with children would also prove valuable in terms of being able to compare the data we collect with children from what we gather in adults. Therefore helping us to elucidate any differences in neuropsychological profile between children and adults with AN. This review is the first to our knowledge to summarise the current state of the literature in young age group with AN. Clarifying the literature in this way will be beneficial not only for future research (in terms of methodological recommendations), but it will also aid the development of future treatments. For example Cognitive Remediation Therapy was introduced as intervention within the adult AN population [29] and it is now starting to attract more attention from clinicians working with adolescents [30].

However, it is clear from both the present review and an earlier review of set-shifting abilities in children [10], that a lack of data in this area currently limits us from drawing firm conclusions about the profile of children and adolescents with AN. Further research is therefore needed to firstly confirm the neurocognitive profile of young group with AN, and then secondly to determine whether remedial treatments are required in this population. In conclusion, the present review aimed to provide some clarity in regards to weak central coherence in children and adolescents with AN, and ultimately provide support for the endophenotype hypothesis. The review found a number of studies examining central coherence in children and

adolescents with AN, however it also found a number of methodological constraints that made interpretation difficult. The available data hints that children and adolescents with AN may show inefficient global processing, however it is clear that this is an important area in need of further research, employing robust methodology, in order to confirm this and provide evidence for the endophenotype hypothesis.

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Since the publication of this study there have been three studies examining central coherence in children and adolescents with AN. Rose, Frampton, and Lask (2014) reported no significant differences between AN and HC groups on the order index, style index or central coherence index of the ROCFT. Kjaersdam Telléus et al. (2014) used accuracy and recall scores as a measure of central coherence, and reported no differences in these scores between AN and HC groups. Stedal et al. (2015) also reported no differences in Z scores on the ROCFT between AN or HC groups. Differences in scoring methodology of the ROCFT may have contributed to the null findings in these studies.

1.8.7 Summary of neuropsychological processing in AN

Figure 14 demonstrates the cognitive characteristics contributing to the neuropsychological processing style of adults with AN. Empirical studies have produced a wealth of evidence to confirm that the cognitive processing style of adults with AN is associated with inefficient set shifting and weak central coherence, as well as high IQ (Lopez et al., 2010; Lopez et al., 2008b; Tchanturia et al., 2012b).

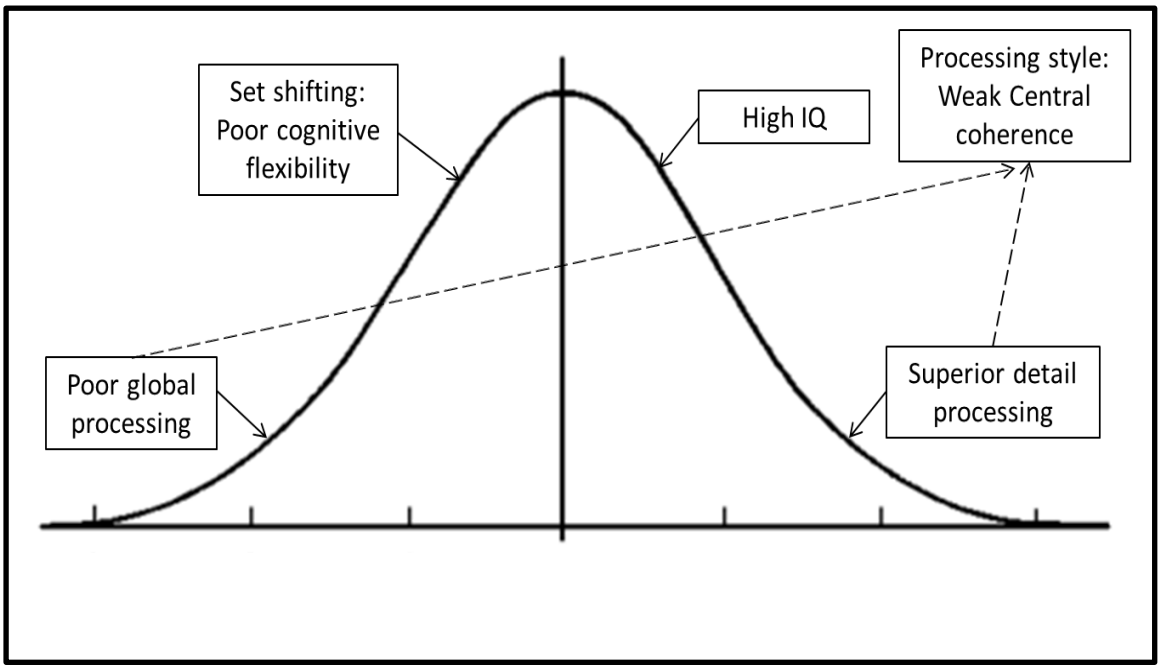

Figure 14: The neuropsychological processing profile of adults with AN.

This profile has also been observed in an attenuated form in individuals who are recovered from the disorder (Harrison, Tchanturia, & Treasure, 2011; Roberts et al., 2010). Inefficient set shifting is also marked in unaffected first-degree relatives of those with AN, and there is evidence of lower levels of holistic processing in these relatives as well (Roberts et al., 2010, 2013). Whether or not weak central coherence is also exhibited in unaffected relatives is yet to be researched. Evidence of an inefficient processing style in children and adolescents with AN is lacking, and the available studies are marred by small sample sizes and other methodological flaws.

Figure 15 depicts a forest plot of a meta-analysis of adult and child and adolescent AN studies that have employed the WCST as a measure of set shifting and have reported perseverative errors on this task.

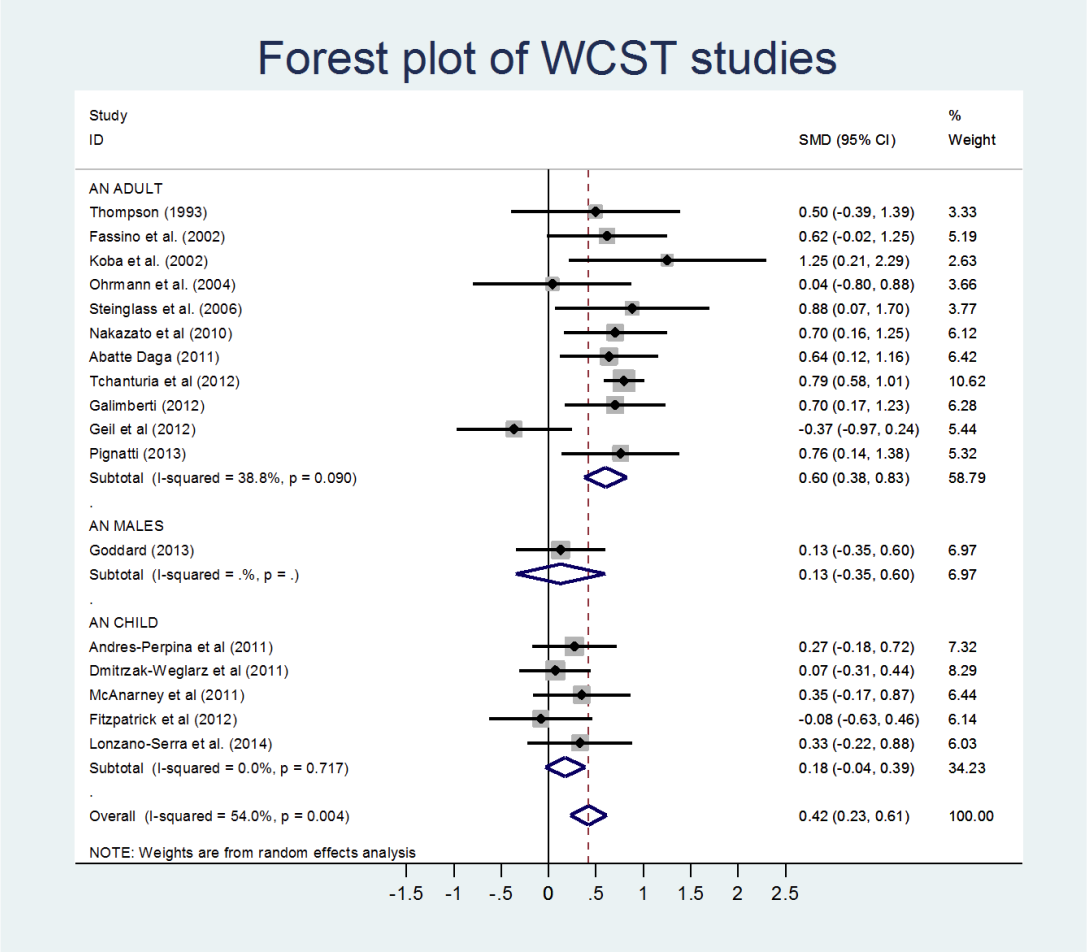

Figure 15 Forest plot of adult and child and adolescent AN studies using the Wisconsin Cart Sorting Test. Taken from Tchanturia & Lang (2014).

This graph demonstrates several important points with regards to the current status of the set shifting literature in AN. Firstly, the graph displays the differences in pooled effect sizes between the child and adolescent AN studies (*d*=0.18) and the adult AN studies (*d*=0.6), suggesting that whilst significant and medium sized differences in performance between AN and HCs are being observed in the adult literature, these are not present to the same extent in children and adolescents.

Secondly, in comparison to the number of adult AN studies, there are a relatively small amount of child and adolescent AN studies utilising the WSCT and reporting perseverative errors with HC comparison groups. Furthermore, the sample sizes within these child and adolescent studies are much smaller than in the adult studies (for child studies the average sample size is: ~N=25, and for adult studies it is: N=~35). The contrast in the number of available studies and the relatively small sample sizes in the child and adolescent AN literature may therefore be contributing to these small effect sizes.

1.9 SOCIO-EMOTIONAL PROCESSING IN ANOREXIA NERVOSA

Socio-emotional processing refers to a number of cognitive and perceptual processes that can inform and guide social behaviour and interaction (Adolphs, 1999).

Historically, there are descriptive accounts associating AN with social and interpersonal difficulties (Bruch, 1962). These accounts are further supported by reports of poor social networks and difficulties in making and sustaining friendships in individuals with AN (Doris, Westwood, Mandy, & Tchanturia, 2014; Hartmann, Zeeck, & Barrett, 2010; Krug et al., 2012; Tchanturia et al., 2013a; Tiller et al., 1997). As these difficulties are believed to occur premorbidly, and are also a predictor of poor treatment response, several models suggest that they are core features of the disorder (Connan et al., 2003; Treasure & Schmidt, 2013). The current literature in regards to socio-emotional processing will be reviewed in the following section.

1.9.1 Socio-emotional processing in adults with Anorexia Nervosa

1.9.1.1 Alexithymia

Alexithymia refers to difficulties with identifying and describing emotional states (Nowakowski, McFarlane, & Cassin, 2013). Studies using self-report measures have demonstrated elevated rates of alexithymia in adults with AN in comparison to HC groups (Berthoz, Perdereau, Godart, Corcos, & Haviland, 2007; Corcos et al., 2000; Troop, Schmidt, & Treasure, 1995), and recent systematic reviews and meta-analyses have confirmed that this is a robust and well replicated finding (Nowakowski et al., 2013; Oldershaw, Lavender, Sallis, Stahl, & Schmidt, 2015). Furthermore, one study also demonstrated higher rates of alexithymia in the AN group as rated by partners or parents (Berthoz et al., 2007). In line with this a recent a meta-analysis of 13 studies by Caglar-Nazali et al. (2014) found higher levels of alexithymia in AN groups with large effect sizes. Rozenstein, Latzer, Stein, and

Eviatar (2011) also found higher levels of alexithymia in unaffected sisters of individuals with EDs.

There is only one published study in the literature investigating alexithymia in recovered ANs, which demonstrated an attenuated profile in the recovered group (Tchanturia et al., 2012a).

1.9.1.2 Recognising emotions in others

There have been mixed results from studies using paradigms to assess the recognition of basic emotions (sadness, happiness, fear and anger, disgust, surprise) and also complex emotions in the eyes (Harrison, Sullivan, Tchanturia, & Treasure, 2009; Kessler, Schwarze, Filipic, Traue, & von Wietersheim, 2006).

Several studies have found no differences in the performance of AN and HC groups on these tasks (Kessler et al., 2006; Mendlewicz, Linkowski, Bazelmans, & Philippot, 2005), whereas others have found poorer performance in AN groups (Castro, Davies, Hale, Surguladze, & Tchanturia, 2010; Harrison et al., 2009; Harrison, Sullivan, Tchanturia, & Treasure, 2010; Jänsch, Harmer, & Cooper, 2009; Kucharska-Pietura, Nikolaou, Masiak, & Treasure, 2004; Oldershaw, Hambrook, Tchanturia, Treasure, & Schmidt, 2010; Pollatos, Herbert, Schandry, & Gramann, 2008; Rozenstein et al., 2011; Russell, Schmidt, Doherty, Young, & Tchanturia, 2009).

Two meta-analyses demonstrated that overall individuals displayed difficulties with emotion recognition tasks but with small effect sizes (d=0.3) (Caglar-Nazali et al., 2014; Oldershaw et al., 2011).

Two studies have also investigated facial emotion recognition in individuals who have recovered from AN. Oldershaw et al. (2010) reported an intermediate profile between AN and HC, whereas Harrison, Tchanturia, and Treasure (2010) data suggests that these difficulties are present in those recovered from AN.

1.9.1.3 Theory of mind

Theory of mind (ToM) can be described as the ability to infer mental states in others (Baron-Cohen, Leslie, & Frith, 1985; Premack & Woodruff, 1978). Four studies have demonstrated difficulties with ToM using experimental paradigms (De Sampaio et al., 2013; Oldershaw et al., 2010; Russell et al., 2009; Tchanturia et al., 2004b); however, a number of studies have been unable to find any differences between AN and HC groups (Adenzato, Todisco, & Ardito, 2012; Pradas, Pastor, Moya, Touriño, & Llandrich, 2012).

A meta-analysis of 12 studies demonstrated that individuals with AN performed significantly worse than HCs on tasks requiring inferring mental states, with large effect sizes (*d*=0.7, (Caglar-Nazali et al., 2014)).

Four studies examined ToM in recovered ANs, and despite some individual study variations, a meta-analysis of these studies suggested an intermediate profile between full AN and HCs (*d*=0.09, (Caglar-Nazali et al., 2014)), suggesting that these difficulties may be present in individuals who have recovered from AN, and may be further exacerbated by starvation.

1.9.1.4 Emotion expression

There is now consistent evidence to suggest that individuals with AN possess altered facial emotion expression. Soussignan, Jiang, Rigaud, Royet, and Schaal (2010) found that individuals with AN produced significantly less positive emotion expressions whilst viewing pictures of food stimuli in comparison to HCs. However, there were no differences between the groups in the amount of negative facial expressions between AN and HC groups.

Reduced emotion expressivity in AN has also been demonstrated in relation to non-food related stimuli. Davies, Schmidt, Stahl, and Tchanturia (2011) found reduced emotion expression in AN in response to both positive and negative film clips.

Furthermore, they also found that the AN group looked away from the negative stimuli significantly more than the HC group, postulated to reflect an attempt to avoid the negative stimuli or self-regulate negative emotions as a consequence of viewing the film. Similarly, Claes et al. (2012) observed that although AN participants reported feeling higher levels of baseline anger whilst participating in a therapeutic video game, they did not display signs of anger facially. Cardi et al. (2014) observed fewer facial emotion expressions in a group of ED participants in response to films of smiling infants than in the HC group, despite reporting the same levels of positive emotions subjectively.

The most recent study of emotion expression specifically explored the expression of positive emotions through examination of the Duchenne smile (a spontaneous smile associated with genuine pleasure, characterised by movements around the corner of the eyes and lips, (Darwin, 1872)) in individuals with AN, BN and HCs. Individuals with AN displayed Duchenne smiles for significantly shorter periods of time in comparisons to the BN and HC groups, and the smiles were also of lower intensity (Marin Dapelo et al., in press).

A second study by Davies, Schmidt, and Tchanturia (2013) using the same experimental paradigm as their 2011 study, demonstrated an attenuated profile in individuals recovered from AN, suggesting that it could represent an underlying trait, exacerbated by starvation.

1.9.2 Socio-emotional processing in children and adolescents with Anorexia Nervosa

There are currently a limited number of studies investigating socio-emotional processing in children and adolescents with AN.

1.9.2.1 Alexithymia

Only one study has examined alexithymia in children and adolescents with AN. Zonnevijlle-Bendek, Van Goozen, Cohen-Kettenis, Van Elburg, and Van Engeland (2002) demonstrated higher levels of alexithymia in children with AN compared to HC groups.

1.9.2.2 Recognising emotions in others

Zonnevylle-Bender, Van Goozen, Cohen-Kettenis, van Elburg, and Van Engeland (2004) found that children and adolescents with AN were significantly worse at an experimental measure of facial emotion recognition than HCs. In a follow-up study, the same authors demonstrated a comparable performance on a measure of emotion recognition between adults and children and adolescents with AN (Zonnevylle-Bender et al., 2004).

1.9.2.3 Theory of Mind

There is only one study in the published literature examining ToM in children and adolescents with AN. Schulte-Rüther, Mainz, Fink, Herpertz-Dahlmann, and Konrad (2012) used functional Magnetic Resonance Imaging (fMRI) to examine brain activation during participation in a behavioural measure of ToM. Although they found no differences in performance on the ToM task (the authors attributed this to

the task being less sensitive in nature), differences in patterns of brain activation between the groups were observed. The AN groups was characterised by hypoactivation of several brain areas believed to be important for ToM such as the medial prefrontal cortex and the temporal cortex. Furthermore, this aberrant brain activity persisted following weight restoration, leading to the suggestion that it could represent an underlying social-cognitive phenotype.

1.9.2.4 Emotion expression

Currently, there is one published study investigating emotion expression in children and adolescents with AN. In a replication of the research paradigm used by Davies et al., (2010), Rhind, Mandy, Treasure, and Tchanturia (2014) found altered emotion expression to both positive and negative film clips in children and adolescents with AN, suggesting they may share the same difficulties with the production of emotion expression as the adult population.

1.9.2.5 Summary of socio-emotion processing in AN

Experimental studies have provided empirical evidence that adults with AN demonstrate difficulties across a number of areas of social cognitive processing. These difficulties appear in an attenuated form in individuals who have recovered from AN, and seem to be exacerbated further by starvation. Data are mixed from studies assessing emotion recognition through faces, though there is strong evidence of altered facial emotion expression in adults. Although limited in number, the preliminary studies assessing socio-emotional processing in children and adolescents with AN suggest a similar pattern of difficulties; however, further studies are required to confirm this.

1.10 TYPICAL BRAIN DEVELOPMENT

Adolescence is a period of significant development in brain structure, function and cognition. In the context of this thesis, it is also important consider the typical developmental trajectory of neuroanatomical and functional changes, as well as the typical development of both cognitive and socio-emotional functions.

1.10.1 Structural development

The human brain continues to develop structurally from birth and into early adulthood with significant changes to both white and grey matter volumes (Shaw et al., 2008). Linear increases in white matter due to neuronal myelination take place throughout multiple brain regions (Blakemore & Choudhury, 2006; Giedd et al., 1999). However, non-linear region-specific changes to grey matter volume also take place. Increases in grey matter, termed synaptogenesis take place throughout numerous brain regions, reflecting differential rates of maturation (Giedd et al., 1999; Giorgio et al., 2010).

Cognitive control functions such as set shifting are thought to be mediated by fronto-striatal brain circuits (Sowell, Thompson, Tessner, & Toga, 2001). Similarly social cognition is also mediated by prefrontal areas (Blakemore & Choudhury, 2006). Findings from neuroimaging studies have shown that these areas mature later than regions involved in more basic cognitive abilities (Marsh, Maia, & Peterson, 2009). Prolonged increases to grey matter volume in these prefrontal areas take place during preadolescence, peaking around 11-12 years of age. This is followed by decreases in grey matter, reflecting the process of synaptic pruning, whereby a number of synapses are discarded (Giedd et al., 1999; Sowell et al., 2001). Such organisational changes in grey matter are thought to underlie increases in neuronal efficiency that is observed over different developmental stages (Blakemore, 2012a).

1.10.2 Functional development

Findings from fMRI studies have consistently demonstrated differential patterns of brain activity between children, adolescents and adults when performing both cognitive and socio-emotional tasks, suggesting a pattern of developmental trajectory for tasks requiring executive functions and higher order cognitive processes and control, such as inhibition and cognitive flexibility. Numerous fMRI studies have demonstrated that children show elevated brain activation in ventral and dorsal prefrontal areas compared to adults (Casey, Galvan, & Hare, 2005; Casey, Tottenham, Liston, & Durston, 2005).

Similarly, there is consistent evidence from fMRI studies of distinct patterns of brain activation in brain areas known to be implicated in the processing of social information in different age groups. A number of studies have demonstrated greater activity in the Dorso-Medial Prefrontal Cortex (dMPFC) during mentalisation tasks in children and adolescents compared to adults (Blakemore, den Ouden, Choudhury, & Frith, 2007).

The structural changes described above are thought to underpin this differential pattern of activity, whereby neuronal myelination and synaptic pruning may lead to the employment of differential and more efficient processing strategies (Blakemore, 2012b; Marsh et al., 2009)

1.10.3 Cognitive and socio-emotional development

Developmental changes are also demonstrated in the performance of experimental tasks measuring executive function and social cognition. There is evidence of continued development of performance into late adolescence (Blakemore & Choudhury, 2006; Romine & Reynolds, 2005). The changes to brain structure and function in prefrontal and parietal areas throughout childhood and adolescence are thought to mediate these changes in performance.

A meta-analysis of five studies examining the developmental trajectory of cognitive flexibility using the WCST demonstrated that the greatest period of development for this function was between five and eight years of age, with continued development between eight and 11 years. There were small increases between 11-14 years, and then no further changes in ability during this time (Romine & Reynolds, 2005).

Social behaviour and performance on socio-emotional processing tasks is likely to be influenced by a complex interaction between an increase in social experiences and opportunities throughout childhood and adolescence, and the development and maturation of the neural systems involved in emotion processing (Blakemore & Choudhury, 2006). A continuum in the development of socio-cognitive behaviour through development reflects this process (Herba & Phillips, 2004).

1.11 ENDOPHENOTYPES

The evidence gathered from experimental studies regarding the neuropsychological profile and the socio-emotional difficulties in those currently ill with AN, recovered from AN and their unaffected relatives, as well as preliminary evidence of a genetic link has led to the suggestion that they may represent endophenotypes for AN.

Endophenotypes (also known as intermediate phenotypes) refer to biological traits that lie somewhere between the genetic susceptibility for a disorder and its phenotypic characteristics (Gottesman & Gould, 2003). Elucidating endophenotypes can offer insights into the possible genetic underpinnings of a particular disorder by providing more accurate targets for candidate genetic studies. Endophenotypes are quantitative measurements, and there are certain criteria that a trait must fulfil to be defined as an endophenotype:

1. It must occur at a higher rate in the affected population
2. It must be present in the affected population regardless of illness status (i.e. even if the individual is in remission).
3. It must be heritable.
4. It must occur in unaffected family members at a higher rate than in the general population.

If a trait fails to demonstrate a genetic element then is it more accurately defined as a biomarker than an endophenotype.

Although the ED field has some evidence of cognitive and social emotion difficulties in currently ill and recovered populations, as well as emerging evidence of a genetic link, the available data from the child and adolescent population is highly inconsistent. The literature reviewed as part of this thesis highlights the need for larger experimental studies with children and adolescents to confirm their neuropsychological and socio-emotional profile. Such data would contribute to our understanding of whether these may be underlying traits in AN as, theoretically, the effects of starvation on these characteristics in patients with shorter illness durations should be less pronounced.

1.12 HOW HAS THIS RESEARCH INFORMED THE TREATMENT OF AN?

The wealth of research implicating both cognitive processing style and socio-emotional difficulties in AN has translated into clinical practice and provided targets for new treatments for AN.

1.12.1 Cognitive Remediation Therapy

Observations of this inefficient processing style in AN has led to the development of Cognitive Remediation Therapy (CRT) for AN (Tchanturia, Lloyd, & Lang, 2013b). CRT has been used successfully with patients with brain lesions and schizophrenia (Cicerone et al., 2011; Wykes et al., 2003). However, CRT for AN has a different focus to these other disorders, and has required some adaptation. The discovery of inefficient set shifting and WCC in adults with AN had provided specific targets for CRT for AN, and the treatment involves participating in a number of cognitive tasks aimed at improving flexible and 'bigger picture' thinking, as well as discouraging perfectionist tendencies. CRT uses meta-reflection, encouraging the patient to reflect on the strategies they employed to complete each task, and consider their own strengths and weaknesses in their cognitive profile. A motivation style of delivery is used to try and engage the patient in treatment (Tchanturia, 2014).

Evidence from RCTs has also shown improvements to cognitive functioning following individual treatment intervention (Brockmeyer et al., 2014; Dingemans et al., 2013; Lock et al., 2013; Tchanturia, Lounes, & Holttum, 2014b), and there is data to suggest it is also well received in a group format (Genders & Tchanturia, 2010; Pretorius et al., 2012).

Preliminary data has been collected demonstrating its use with children (Dahlgren, Lask, Landrø, & Rø, 2013; Noort, Kraus, Pfeiffer, Lehmkuhl, & Kappel, 2015; Wood, Al-Khairulla, & Lask, 2011). However further clarity is needed regarding the neuropsychological processing profile of younger populations with AN before possible treatment targets for young people with AN can be confirmed.

1.12.2 Cognitive Remediation and Emotion Skills Training

Cognitive remediation and emotion skills training (Money, Davies, & Tchanturia, 2011) (CREST), is a treatment module that places an emphasis on management and expression of emotions, as well as positive emotion recognition skills (Tchanturia, Doris, & Fleming, 2014a). It is based on the maintenance model of AN (Treasure & Schmidt, 2013) and aims to increase the patient's quality of life by increasing awareness of emotions and social communication skills (Money et al., 2011).

1.12.3 The Maudsley Model of Anorexia Nervosa Treatment for Adults

The Maudsley Model of Anorexia Nervosa Treatment for Adults (MANTRA) is a therapy that also draws on the empirical findings of neuropsychological and socio-emotional processing studies in AN. It is based on the cognitive interpersonal maintenance model of AN and focuses on biological and trait factors important to the aetiology and maintenance of AN, such as neuropsychology, socio-emotional processing and personality aspects. It is manualised and modulised, meaning that it can tailor to the needs of each individual patient. However, the main outcome of MANTRA differs from CRT, and its main focus is recovery from ED symptoms and weight-restoration. Initial results from a pilot study were promising, with significant improvements in BMI and other ED associated pathology, (Wade, Treasure, & Schmidt, 2011); however, a more recent RCT comparing MANTRA to SSCM did not indicate that MANTRA was a superior treatment for AN (Schmidt et al., 2012).

1.13 AIMS AND HYPOTHESES OF THESIS

The overall aim of this thesis is to investigate neuropsychological and socio-emotional processing in children and adolescents with AN and to improve our understanding of these mechanisms that are likely to be important in both the pathogenesis and maintenance of AN. The thesis is presented as a series of studies, with separate aims and hypotheses. These are presented in table 6.

Study	Aims	Hypotheses
STUDY 1: Do children and adolescents with AN display an inefficient cognitive processing style?	To investigate the neuropsychological profile of children and adolescents with AN, by assessing set shifting and central coherence.	Children and adolescents with AN will demonstrate higher levels of perseveration on a measure of set shifting, and lower levels of global processing on measures of central coherence.
STUDY 2: Is inefficient cognitive processing in Anorexia Nervosa a familial trait? A neuropsychological pilot study of mothers of offspring with diagnosis of AN.	To investigate the neuropsychological profile of unaffected mothers of offspring with AN.	Unaffected mothers of children and adolescents with AN will demonstrate poorer set shifting and lower levels of global processing on measures of central coherence compared to mothers of HC children and adolescents.
Study 3: Acceptability and feasibility of self-help CRT for AN delivered in collaboration with carers: A qualitative preliminary evaluation study.	To assess the feasibility and acceptability of a self-help CRT manual for use in collaboration with carers.	As this study is exploratory there is no directional hypothesis.
Study 4: Exploring emotion recognition in adults and adolescents with AN using a body motion paradigm.	i. To investigate emotion recognition through body motion in a large sample of participants with AN using the PLW task. ii. To investigate developmental differences in emotion recognition abilities in AN.	Participants with AN will perform poorer than HCs on a measure of emotion recognition through body motion.
Study 5: Emotion expression and associated clinical factors in children, adolescents and adults with AN	i. To investigate emotion expression in an age diverse group of individuals with AN; ii. To investigate demographic and clinical correlates of emotion expression within the AN group.	i. Participants with AN will demonstrate altered emotion expression in response to film clips designed to evoke emotion. ii. Altered emotion expression will be associated with a number of demographic and clinical variables (e.g. age, BMI).

Table 6: Separate aims and hypotheses for each study.

CHAPTER 2

GENERAL METHODS

2.1 OVERVIEW

The details of each study's specific methodology (e.g. the procedure) can be found within each of the study manuscripts or chapters. This chapter aims to provide a general overview of the methodology employed in this thesis, and provide additional details not included in the individual manuscripts.

2.2 DESIGN

Studies 1, 2, 4 and 5 employed a cross-sectional design incorporating quantitative experimental measures. Study 3 was a pilot acceptability and feasibility study of an intervention and therefore employed both quantitative and qualitative measures, pre- and post- intervention.

2.3 PARTICIPANTS

2.3.1 Inclusion and exclusion criteria

The inclusion and exclusion criteria for each study are shown in tables 2.1-2.4

AN	HC
Inclusion	
Primary diagnosis AN	No past / current ED / psychiatric symptoms, no family history ED
% IBW < 90	%IBW> 90
Aged 11 - 18	Aged 11 - 18
Fluent in English	Fluent in English
Exclusion	
% IBW >90 (weight restored)	%IBW <90
Severe medical disorder	%IBW > 120 (obese range)
Psychotic disorder	Clinical levels of psychiatric symptoms
	Current / past ED symptoms
	Family history of ED
	Severe medical disorder
	Psychotic disorder

Table 1: Inclusion/exclusion criteria for study 1: Do children and adolescents with Anorexia Nervosa display inefficient cognitive processing?

AN mother	HC mother
Inclusion	
Mother of AN participant taking part in study	Biological mother of HC participant taking part in study
No past / current eating disorder symptoms (unaffected)	No past / current ED / psychiatric symptoms, no family history ED
BMI > 18.0	BMI > 18.0
Fluent in English	Fluent in English
Exclusion	
BMI < 17.5	BMI < 18.0
Diagnosis / symptoms of eating disorder	BMI > 30 (obese range)
Severe medical disorder	Current / past ED symptoms
	Severe medical disorder
	Psychotic disorder

Table 2: Inclusion/exclusion criteria for study 2: Is inefficient cognitive processing in Anorexia Nervosa a familial trait? A neuropsychological pilot study of mothers of offspring with diagnosis of anorexia nervosa.

Inclusion
Both an offspring with a diagnosis of Anorexia Nervosa or EDNOS-AN (in-line with DSM IV) and their mother willing to participate.
Offspring aged between 12-40 years of age.
Exclusion
Mother unable to participate.
Brain injury.
Not fluent in English.
Learning disability.
Psychotic disorder.

Table 3: Inclusion/exclusion criteria for study 3: Acceptability and feasibility of self-help Cognitive Remediation Therapy for Anorexia Nervosa delivered in collaboration with carers: A qualitative preliminary evaluation of a pilot study.

AN	HC
Inclusion	
Primary diagnosis AN	No past / current ED / psychiatric symptoms, no family history ED
BMI < 17.5 / % IBW < 90	BMI > 18.0 / %IBW > 90
Aged 11 - 55	Aged 11 - 55
Fluent in English	Fluent in English
Exclusion	
BMI > 17.5 / % IBW >90 (weight restored)	BMI < 18.0 / %IBW <90
Severe medical disorder	BMI > 30 / % IBW > 120 (obese range)
Psychotic disorder	Clinical levels of psychiatric symptoms
	Current / past ED symptoms
	Family history of ED
	Severe medical disorder
	Psychotic disorder

Table 4: Inclusion/exclusion criteria for studies 4 and 5: Exploring Emotion Recognition in Adults and Adolescents with Anorexia Nervosa Using a Body Motion Paradigm AND Emotion expression and associated clinical factors in children, adolescents and adults with Anorexia Nervosa.

2.3.2 Recruitment

Children and adolescents with AN were recruited from the day programme or outpatient service of Child and Adolescent Eating Disorder Service, South London & Maudsley NHS Trust. Adults with AN were recruited from the outpatient or inpatient eating disorder services at the South London & Maudsley NHS Trust and the Vincent Square Eating Disorder service, Central and North West London NHS Trust. All AN participants had a diagnosis of AN according to DSM-IV criteria, which was in force at the time of recruitment. All AN participants had received their diagnosis from their clinical team.

Healthy control children and adolescents were recruited from local schools, colleges and advertisements in the local community. Similarly, the HC adults recruited for studies 4 and 5 were recruited from advertisements in the local community. All HC participants were screened for the possible presence of psychiatric disorders using a psychiatric screening tool and self-report questionnaires. Participants were excluded from the study if their scores were elevated on any of these measures.
The unaffected mothers and healthy control mothers recruited as part of study 2 were a sub-sample of mothers of children and adolescents that had taken part in the larger neuropsychological study.

The families who participated in study 3 were recruited from advertisements on the eating disorder charity Beat's website (www.b-eat.co.uk), eating disorder support groups and the Child and Adolescent Eating Disorder Team, South London & Maudsley NHS Trust.

All of the participants across the studies included in this thesis were female. The sample sizes varied between each individual study and these details can be found in the respective papers.

2.4 ETHICAL APPROVAL

Ethical approval was sought and obtained from the Dulwich Research and Ethics Committee, as well as receiving Research and Design approval from the South London and Maudsley NHS Trust. The ethical approval number of this study is 12/LO/2015.

2.5 MEASURES

2.5.1 Demographic measures

2.5.1.1 Weight and height

For children and adolescents (participants aged 18 years or under) height and weight measurements were used to calculate a percentage of each participant's ideal body weight (%IBW). This measurement was corrected for age and gender. For studies in which adults were included (19 years and over), weight and height data were used to calculate a Body Mass Index (BMI, kg/m^2).

2.5.1.2 Socio-demographic questionnaire

Socio-demographic data was collected for all participants regarding: age, gender, occupation, marital status, education, medication and family psychiatric history. For participants in the AN groups there were also additional questions relating to length of illness and treatment history.

2.5.1.3 Psychiatric screening tool

The Structured Clinical Interview for DSM-IV (SCID, (First, Spitzer, Gibbon, & Williams, 2012) screening questionnaire was implemented to screen for the presence of possible psychiatric illnesses within both the AN and HC groups. The SCID is a semi-structured interview that probes for symptoms of depression, anxiety, OCD, substance abuse and eating disorder pathology. It is widely used and recommended for research protocols in psychiatric populations.

2.5.2 Neuropsychological measures

2.5.2.1 Intelligence Quotient (IQ)

The Wechsler Abbreviated Scale of Intelligence (WASI, (Wechsler & Hsiao-pin, 2011) was employed as a measure of IQ for all study participants. The WASI is formed of four sub-scales assessing both performance (block design and matrix reasoning) and verbal intelligence (vocabulary and similarities). The performance IQ (PIQ) and verbal IQ (VIQ) scales are combined to produce a Full Scale IQ (FSIQ). The WASI is well validated with established normative data (Ryan et al., 2003; Wechsler & Hsiao-pin, 2011) and is known to have good psychometric properties, such as factor structure and construct validity (Canivez, Konold, Collins, & Wilson, 2009; Hays, Reas, & Shaw, 2002).

The inclusion of the WASI strengthened the study in several ways. Firstly, the WASI can be used with individuals from the age of 6 to 89, and requires approximately 30 minutes to administer. It therefore provides a time-efficient multi-dimensional measure of intelligence that can be used across the age span.

Secondly, in neuropsychological studies it is of great importance to ensure that both the psychiatric and the HC groups are matched in regards to IQ. Once IQ is comparable across the group it raises confidence in attributing any differences in task performance specifically to the aspect of processing one is testing, and not to differences in IQ.

2.5.2.2 Set shifting

The Wisconsin Card Sorting Test Computer Version 4 (WCST, (Heaton, 1993) was employed as a measure of set shifting in this study. A detailed description of the procedure of this task can be found in chapter 3 (page 124). Historically this task was administered manually using a deck of cards (Grant & Berg, 1948). However, a computer version has since been created, allowing for a standardized measure and reducing the possibility of experimenter error or bias (Heaton, 1993).

The WCST is a multi-dimensional tool, tapping into numerous areas of executive function such as working memory, impulse control and reward, and it is therefore not regarded as a 'pure' measure of set shifting. However, the computerised output produced by the WCST provides numerous different outcomes, including measures of general performance, perseveration, conceptual ability and response consistency, therefore providing a separate measure of each domain.

The most relevant measure in relation to set shifting ability is the number of perseverative errors made by the participant. The WCST reports perseverative errors as a raw score and a percentage. This study has chosen to report percentage perseverative errors as the main outcome for set shifting. This is because the number of cards dealt to each participant can vary depending on the number of errors (perseverative or otherwise) a participant makes (higher number of errors will result in more cards being dealt). Using percentage perseverative errors therefore provides a standardized measure across all participants, regardless of each individuals overall performance.

As well as reporting the perseveration outcomes, study 1 also reported the other measures provided by the WCST, in order to render the results comparable with the largest study in the adult AN field (Tchanturia et al., 2012b). The present study replicated the test parameters of Tchanturia et al. (2012b), whereby visual and audio feedback is given in a male voice one second after each sort (Appendix 10.13). The WCST was chosen to measure set shifting in the present study after careful consideration and review of the adult AN literature highlighted differences between AN and HC groups on this task with medium effect sizes (Roberts et al., 2007; Tchanturia et al., 2012b). Furthermore an exploratory meta-analysis had indicated that with a large sample size, differences may also be witnessed on this task in children and adolescents with AN.

2.5.2.3 Central Coherence

This study employed two neuropsychological tasks to assess central coherence.
The Rey Osterrieth Complex Figures Test (ROCFT) (Osterrieth, 1944)) is a pencil and paper task commonly used in both the ED and wider psychiatric field as a measure of holistic processing.

The drawing strategy adopted by the participant is used as a measure of central coherence, and performance is benefitted from taking a more global approach. The ROCFT in this thesis was scored according to Booth's (2006) scoring method, which incorporates both the order in which the participant chooses to draw the elements (whether preference is shown to global or detailed elements) and the style in which they are drawn in (fragmented or coherently). Order index (OI) and style indexes (SI) are computed and added to give the Central Coherence Index (CCI). Booth's (2006) scoring method is hierarchical, whereby higher scores are awarded when preference is shown to global elements. Higher scores on this measure are indicative of better global or holistic processing (Booth, 2006).

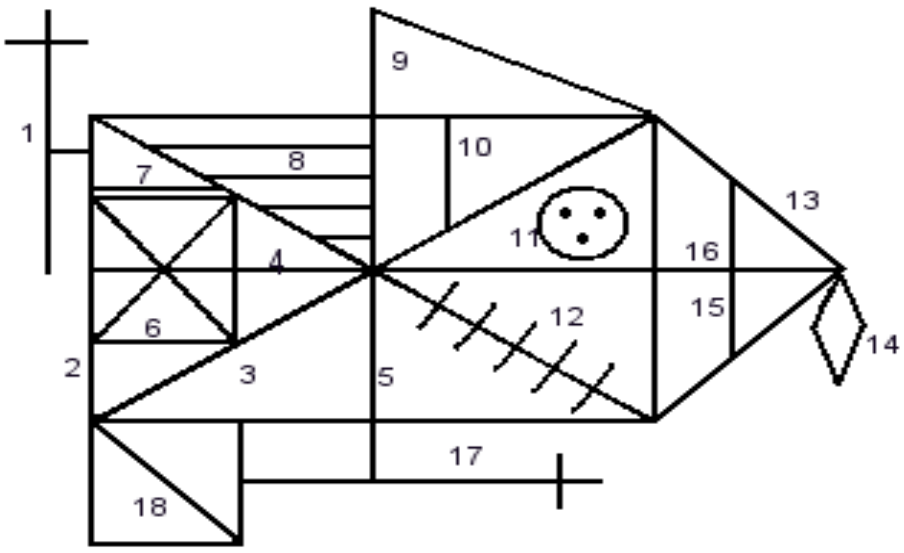

Figure 1: Scoring elements for the Rey Osterrieth Complex Figure Test

Category	Element	Description
Global element (Score=4)	2	Large rectangle
	13	Side of large triangle attached to large rectangle
Global internal element (Score=3)	3	Diagonal cross
	4	Horizontal midline of large rectangle
	5	Vertical midline of large rectangle
	16	Horizontal line with sides of large triangle
Local perimeter element (Score=1)	1	Vertical cross
	9	Small triangle above large rectangle
	14	Diamond
	17	Horizontal cross
	18	Square attached to large rectangle
Local internal element (Score=0)	6	Small rectangle
	7	Small horizontal line above small rectangle
	15	Vertical line within side of large triangle
	8	Four parallel lines
	10	Small vertical line with large rectangle
	11	Circle with three dots
	12	Five parallel lines

Table 5: Scoring system for Rey Osterrieth Complex Figure Test according to Booth (2006).

This scoring method was chosen over other scoring methods, such as delayed recall, as it is now believed to be the most 'direct' measure of central coherence (Booth, 2006) see (Lopez et al., 2008a)) for more details). Furthermore, it replicates the scoring methods adopted by the large adult AN studies and studies from the wider psychiatric field (such as the ASD field, (Happé, 2013), allowing for comparison.

In order to check reliability, 15% of the entire sample was co-rated by a second rater. Interrater reliability was good with Cohens kappa = 0.71, p = < .001.

The fragmented pictures task (FPT, (Snodgrass, Smith, Feenan, & Corwin, 1987)) was also used to measure global processing. The FPT is a computerised task in which participants are presented with a picture that slowly develops frame-by-frame. Participants are asked to indicate verbally what the object is as quickly as possible. There is one practice trial followed by six test trials. The main outcome measure is the mean frame in which the participant correctly identifies the picture. The task is also benefited from a global approach and quicker responses are indicative of a more holistic processing style. An example trial for the FPT can be found in appendix 10.14.

This measure has not been used with child and adolescent AN population, but adults with AN have been shown to perform poorly on this task (Harrison, Tchanturia, Naumann, & Treasure, 2012). Therefore the current study included this measure, alongside a well-established measure of central coherence (ROCFT), to allow for the novel testing of children and adolescent's performance on this task.

2.5.3 Socio-emotional processing measures

2.5.3.1 Emotion Recognition through body motion (Johansson, 1973)

The Pointlight walkers task was used to assess the ability to recognise different emotional states through body motion. It is a computerised task involving short film clips of actors walking from the left side of the screen to the right, whilst portraying one of four emotional states (happiness, sadness, anger or fear) or a neutral state. The actors were filmed in the dark with small lights attached to each joint (wrists, ankles, shoulders, knees and hips) and their head; therefore participants observed white dots on a black background giving the appearance of a human body without any facial features. A still image of the Pointlight walkers task is presented in figure 2, and an example clip of 'fear' can be viewed at: http://www.wjh.harvard.edu/~heberlein/CF36.qt

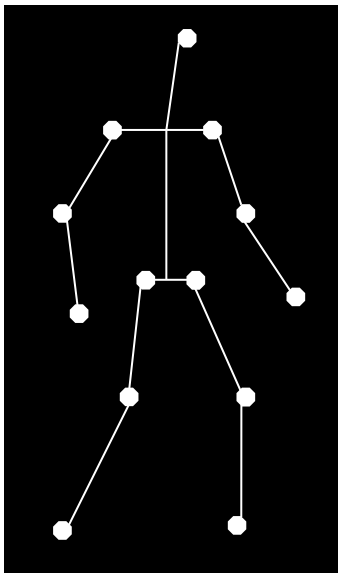

Figure 2: Still image of Pointlight walker, taken from Brittain and Surguladze (2012). Lines joining the dots are for illustration only.

The task consisted of 40 trials in total, made up of eight clips for each emotion plus eight neutral clips. For each trial participants selected which emotion they believed was being portrayed from a forced-choice answer sheet. In addition to the 40 trials, all participants underwent five practice trials in which they observed a clip of each emotion and a neutral clip.

In line with previous studies, this study employed a proportional scoring method (Heberlein, Adolphs, Tranel, & Damasio, 2004). In a pilot study, 15 'reference' HC participants rated the emotional clips in the way described above, with the exception that there were no 'neutral' clips and no 'neutral' answer choice (i.e. 32 clips). Percentages were calculated for the number of times each stimulus was labeled as a particular emotion by the reference group. These percentages then formed the basis of the partial correctness scoring for the main study. For example, if a clip was labeled as 'happy' by 70% of the reference group, 'angry' by 20% of the reference group, and 'sad' by 10% of the reference group, then if a participant in the main study labeled the same clip as 'happy' they would achieve the highest score of 1.0 (0.7/0.7), if they labeled it as 'angry' they would score 0.28 (0.2/0.7), and if they labeled it as 'sad', they would score 0.14 (0.1/0.7). All other answers would receive a score of 0. In the main study, the total score for each emotion corresponds to the sum of the scores obtained by the participant on each of the eight clips that represent the emotion (i.e. the maximum score is 8 for each emotion category). This scoring method accepts that a certain degree of variability in the interpretation of emotions from body movements is common, for example a body movement can be perceived as both sad and fearful (Heberlein et al., 2004).

To date, there is only one study that has implemented this task in an AN population (Zucker et al., 2013). Therefore the inclusion of this paradigm in the present study allowed for the novel testing of children and adolescents, as well as applying it to a large sample size.

2.5.3.2 Film Clips Task Experimental Stimuli

The current study employed the same experimental methodology as described in (Davies et al., 2011). Participants were presented with short film clips designed to evoke positive or negative facial emotion expression. The positive film clip was a scene from the comedy film 'Four Weddings and a Funeral' and the negative film clip was a scene from the film 'Shadowlands'. Please see appendix 10.15 for still images of the film clips. Each film clip was approximately three minutes in duration. Participants' faces were filmed (with their prior knowledge) whilst observing each of the film clips, and these recordings were later coded for emotion expression. Participants were presented with a neutral film clip of simulated waves before and after each of the emotive clips. Facial expression during the neutral film clip was not coded, as the purpose of this clip was to obtain a baseline for facial affect and to eliminate possible carry-over effects produced by the two emotion-inducing film clips.

2.5.3.3 Facial Expression Coding System (FACES, Kring & Sloan, 2007)

The Facial Expression Coding System (FACES, (Kring & Sloan, 2007) was used to examine emotion expression. The FACES is based on the Facial Action Coding System (FACS, (Ekman & Friesen, 1978) a reliable standardised system for coding facial expressions based on the anatomy of emotions, providing rich information about the participant's emotional response. FACES is a global rating system, defining an expression as any change in the face from neutral to non-neutral and then back to neutral. Expressions are only defined as 'positive' or 'negative', and are not assigned a more definitive label (e.g. happiness). Each expression is coded for valence (positive or negative), intensity (1-4) and duration (seconds). A frequency count for each time the participant looks away during the clip is also coded.

Two researchers independently rated the clips. The Kappa for the two researchers was .70 (substantial agreement) for the positive film clip and .90 (perfect agreement) for the negative film clip.

2.5.4 Self-report measures

2.5.4.1 Eating Disorder Examination Questionnaire (EDE-Q; (Fairburn & Beglin, 1994))

A measure of eating disorder psychopathology, 36-item scale scored on a 7-point Likert scale. The measure provides an overall global score and four sub-scales assessing weight, shape concerns, eating concerns and restriction. The EDE-Q has demonstrated good psychometric properties with high internal consistency (Peterson et al., 2007) and reliability (Berg, Peterson, Frazier, & Crow, 2012). The present study used the clinical cut-off of a global score of 2.7 (Mond, Hay, Rodgers, & Owen, 2006; Mond, Hay, Rodgers, Owen, & Beumont, 2004).

2.5.4.2 Hospital Anxiety and Depression Scale (HADS, (Zigmond & Snaith, 1983))

As both symptoms of depression and anxiety are known to occur at a high rate in AN populations, the HADS was used to measures these symptoms. The clinical cut offs as stated in the original paper are: 0-7 non-case, 8-10 possible case, 11-21 probable case. The HADS was chosen as it has shown to be a reliable measure of both symptom severity and caseness. It has also demonstrated good psychometric properties such as factor structure, discriminate and concurrent validity and internal consistency (Bjelland, Dahl, Haug, & Neckelmann, 2002).

2.5.4.3 Obsessive-Compulsive Inventory (OCI, (Foa et al., 2002))

Due to the high comorbidity rate between AN and OCD and the association between these symptoms and poor AN prognosis, it was important to incorporate a measure of OCD within the current study. The OCI was chosen to measure these symptoms.
The OCI is an 18-item scale used to assess the presence and severity of obsessive-compulsive symptomatology. Answers are given on a 5-point Likert scale (0=not at all; 4=extremely), and provide a total score and six sub-scale scores for checking, washing, obsessing, neutralising, ordering and hoarding. Total scores of 21 or above are indicative of clinical obsessive-compulsive behaviour. The OCI has been validated for use with both clinical and non-clinical groups, and also shows good internal consistency in anxious and non-anxious groups (Abramowitz & Deacon, 2006; Foa et al., 2002).

2.5.4.4 Children's Obsessive Compulsive Inventory (ChOCI, (Shafran et al., 2003))

A 44-item measure assessing compulsive and obsessive symptoms in children. A total score of 17 and above is considered to be clinically significant. The ChOCI is known to have good retest reliability and sensitivity (Foa et al., 2010).

2.5.4.5 Autism Quotient-10 (AQ-10, (Allison, Auyeung, & Baron-Cohen, 2012))

There is significant evidence to suggest that many individuals with AN also exhibit higher levels of autistic traits than the healthy population (Gillberg, 1983; Mandy & Tchanturia, 2015; Tchanturia et al., 2013c). There is also a large overlap between these symptoms and poor cognition (Hill, 2004; Treasure, 2013). The current study therefore used the AQ-10 to measure such autistic traits. The AQ10 is a shortened version of the Autism Quotient questionnaire (Baron-Cohen et al., 2001), and consists of 10 items answered on a 4-point Likert scale, ranging from 'definitely agree' to 'definitely disagree'. Scores of 6 or above represent caseness on this measure. The AQ-10 has shown to have good psychometric properties including good specificity, reliability and internal consistency (Allison et al., 2012). Employing the shortened version of this measure reduced burden on participants, whilst maintaining a reliable measurement of these symptoms.

2.5.4.6 Detail and Flexibility Questionnaire (D-Flex, (Roberts, Barthel, Lopez, Tchanturia, & Treasure, 2011))

The DFlex was developed to measure self-reported cognitive style. It is a 24-item measure, whereby answers are given on a 6-point Likert scale (1=strongly disagree; 6=strongly disagree). It provides two sub-scales measuring two aspects of cognitive style: 'cognitive flexibility' and 'attention to detail'. The original paper for this measure reported high internal reliability and construct and discriminant validity (Roberts et al., 2011).

2.5.4.7 Social Anhedonia Scale (SAS, (Chapman, Chapman, & Raulin, 1976)

Levels of social anhedonia (diminished interest or pleasure in most or all social activities) are higher in eating disorder samples than in the normal population (Tchanturia et al., 2012a). The SAS is a well-validated measure of social anhedonia, consisting of 40-items to which patients answer true or false. A score of 12 or above indicates functionally impairing social anhedonia (Pelizza & Ferrari, 2009). This measure has high levels of internal consistency and test-retest reliability (Chapman et al., 1976).

2.5.4.8 Work and Social Adjustment Scale (WSAS, (Mundt, Marks, Shear, & Greist, 2002))

The WSAS is a 5-item measure of impairment of functioning. The clinical cut offs for this measure are: 0-10 subclinical, 10-20 significant functional impairment, >20 moderately severe. It has proven validity and reliability within a number of clinical populations such as OCD, depression and Anorexia Nervosa, and also has good specificity and internal consistency (Mundt et al., 2002; Tchanturia et al., 2013a).

2.5.4.9 Positive and Negative Affect Scale (PANAS, (Watson, Clark, & Tellegen, 1988))

The PANAS was administered to individuals participating in study 5. The PANAS is a 22-item scale, containing items measuring both positive and negative affect. Participants indicate how they currently feel using a 4-point Likert scale for each adjective. The PANAS was completed immediately after viewing each of the emotive film clips. Participants were also asked if they felt any other emotion not listed and if they had seen the film clip before.

2.6 STATISTICAL PLAN

2.6.1 Power calculation

Where possible power calculations were made using the statistical package GPower (Faul, Erdfelder, Lang, & Buchner, 2007) to determine the sample size needed to observe true statistical significance. The sample sizes were based on a power calculation for detecting a medium sized effect with 80% power and a level of significance of 0.01.

For the Wisconsin Card Sorting Test and the Rey Osterrieth Complex Figures Test for study 1 the findings from the adult AN studies of Tchanturia et al. (2012b) and Lopez et al. (2008a) were used as a basis for power calculations.

From the findings of Tchanturia et al. (2012b) it was estimated that that a minimum of 39 participants per group would be needed to detect a group difference on the WCST. For the ROCFT, it was estimated that a minimum of 25 per group would be needed.

Data were not available on set shifting and central coherence in unaffected mothers, and so study 2 employed a pilot study design and a calculation of power was not conducted.

There were no data regarding the Pointlight walkers task and AN, so the outcomes of Brittain and Surguladze (2012) were used to estimate power, estimating that between 50-80 participants would be needed overall .

For study 5, the results of Rhind et al. (2014) were used to estimate how many children and adolescents would be required and Davies et al. (2011) as an estimate of the number of adults needed. From these calculations it was estimated that 33 children and adolescents and 25 adults per group would be needed.

2.6.2 Statistical analysis

For the studies involving quantitative data histograms were used to assess the data for normality. Where data were non-normally distributed log-transformations were conducted to try and normalise the data. For a number of the outcomes log transformations were unable to normalise the data. The learning to learn scale of the WCST and all of the FACES outcomes from study 5 were therefore analysed using the non-parametric Mann Whitney *U* test. Further inspection of the data obtained from study 4 also revealed that there were differences in distributions between the groups in relation to both shape and variability, violating the assumptions of the Mann Whitney U test. This data was therefore analysed using median regression (also known as quantile regression (Cade & Noon, 2003; Koenker, 2005). Median regression is a more robust alternative to linear regression and suitable for modeling skewed data. Standard linear regression estimates the relationship between mean of a response distribution and a set of independent or predictor variables, whereas the median regression models the relationship between median of a response distribution and a set of predictor variables.

Effect sizes are presented throughout this body of work as a standardized measure of difference in performance between AN and HC groups. The measure of effect size presented in these series of studies is Cohen's *d* ($d = (M_{group1} - M_{group2})/SD_{pooled}$), where 0.2=small effect, 0.5=medium effect and 0.8= large effect.

The qualitative data collected as part of study 3 was analysed using thematic analysis (Braun & Clarke, 2006; Joffe & Yardley, 2004), whereby the transcript was read several times and then coded for categories. If a category was mentioned more than once they were then made into broader semantic themes. As a reliability check, a second researcher who was independent of the study was asked to read the transcripts and qualify the themes. They were asked to modify or add any themes they felt had been missed. Both researchers showed agreement, indicating good reliability and consistency of the themes.

CHAPTER 3

STUDY 1: DO CHILDREN AND ADOLESCENTS WITH ANOREXIA NERVOSA DISPLAY AN INEFFICIENT COGNITIVE PROCESSING STYLE?

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PLOS | ONE

RESEARCH ARTICLE

Do Children and Adolescents with Anorexia Nervosa Display an Inefficient Cognitive Processing Style?

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Abstract

Objective

This study aimed to examine neuropsychological processing in children and adolescents with Anorexia Nervosa (AN). The relationship of clinical and demographic variables to neuropsychological functioning within the AN group was also explored.

Method

The performance of 41 children and adolescents with a diagnosis of AN were compared to 43 healthy control (HC) participants on a number of neuropsychological measures.

Results

There were no differences in IQ between AN and HC groups. However, children and adolescents with AN displayed significantly more perseverative errors on the Wisconsin Card Sorting Test, and lower Style and Central Coherence scores on the Rey Osterrieth Complex Figure Test relative to HCs.

Conclusion

Inefficient cognitive processing in the AN group was independent of clinical and demographic variables, suggesting it might represent an underlying trait for AN. The implications of these findings are discussed.

Introduction

Anorexia Nervosa (AN) is an eating disorder (ED) characterised by restriction of calorie intake, problems with weight and shape [1], and carries an extremely high mortality rate [2].

no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing Interests: The authors have declared that no competing interests exist.

Population-based studies have estimated prevalence rates ranging between 1.2–1.9%, and over recent decades there has been an increase in the incidence rates amongst young females (15–19 years), suggesting they represent a particularly high-risk group [3].

AN is also highly associated with obsessive compulsive, perfectionist and social communication difficulties, and such difficulties are postulated to be an intermediate phenotype triggered by a specific neurocognitive profile observed in adults with AN [4]. Inefficiencies with set-shifting (the ability to move flexibly between strategies, rules or behaviours,[5]) and weak central coherence (a bias towards details at the expense of global integration [6]), have been well established in the adult AN literature [7, 8]. These inefficiencies have been found to persist with recovery, with weight-restored individuals displaying an intermediate and attenuated profile [9]. There appears to be a genetic component to this cognitive profile, with it being observed in unaffected relatives of those with eating disorders, such as sisters and healthy offspring of mothers with AN [10, 11]. These findings have led to the postulation that this cognitive style is representative of an endophenotype for the disorder [9, 10, 12]. An endophenotype can be defined as a measureable component between a gene and the observable phenotypic characteristics of a disorder [13].

Neuroimaging studies in the adult AN population have identified structural differences in multiple brain regions in AN cohorts [14, 15]. More recently, functional differences have been identified in participants with AN when completing a central coherence task [16]. Such findings highlight the neural underpinnings that may be linked to the inefficient cognitive processing in AN.

There is evidence from healthy population studies that cognitive processing, and in particular mental flexibility, is important for wellbeing in general [17]. Furthermore it is evident that poor cognitive flexibility and a bias toward detail/poor global integration are risk factors for a range of psychiatric disorders [17], with Obsessive Compulsive Disorder (OCD) and Autism Spectrum Disorder being particularly associated with difficulties in these domains to varying degrees [18, 19]. However there is speculation as to whether such cognitive profiles are only markers for the OCD rather than being underlying endophenotypic traits. Unlike the adult AN literature, evidence of their stability appears to be inconsistent, with some studies showing improvements in cognitive processing following treatment [20, 21], suggesting they could be associated with the acute illness stage, as well as various clinical factors such as severity, symptom dimension and medication use [22, 23]. Results from the child and adolescent OCD studies appear to be conflicting, with one longitudinal study reporting improvement in cognitive processing with the remission of obsessive-compulsive symptomatology [24].

Neuropsychological processing in the child and adolescent AN population has been less widely studied than adult AN, which is surprising considering that neuroimaging studies have highlighted the presence of structural and functional abnormalities in younger AN populations [25].

The available data appears inconsistent, with some studies showing evidence of inefficient processing [26, 27], whilst others are unable to find differences between groups [28–31]. Such inconsistent findings may be due to the heterogeneous nature of the samples recruited in these studies. Systematic reviews of set-shifting and central coherence in children and adolescents with AN highlighted that small sample sizes and large variability in tasks used to assess cognition currently render the available data difficult to interpret [32, 33]. These reviews indicated that although non-significant, there was a trend toward both a more inflexible and a detailed focussed processing style amongst the child and adolescent AN groups. It is therefore clear that this is an avenue worth pursuing with further research, as it would be valuable to clarify the neurocognitive profile of children and adolescents with AN for a number of reasons.

Firstly, elucidating the neuropsychological profile of children and adolescents with AN would be advantageous in the development of more effective treatments for AN. For example, it will help to clarify whether remedial treatments such as Cognitive Remediation Therapy (CRT), which have been found to be effective in the adult AN population are likely to be beneficial in younger patients [34, 35].

Confirming whether or not children with AN show inefficient cognitive processing could contribute evidence to the endophenotype hypothesis and aid our understanding of the neurobiological and genetic underpinnings of AN. It could potentially be used as a marker for subtyping ED's and could help to discriminate AN from other EDs such other specified feeding and eating disorders.

Furthermore once the neuropsychological profile has been defined, this can be merged with our existing knowledge of structural and functional differences to strengthen our understanding of the neural mechanisms involved in AN.

With this in mind, the present study aimed to investigate neuropsychological processing in children and adolescents with AN by comparing their performance on a number of tasks to the performance of healthy controls. We hypothesise that children and adolescents with AN will show a more inflexible processing style and lower global processing abilities compared to their healthy control counterparts.

Material and Methods

Participants

Participants included children and adolescents with a diagnosis of AN (N = 41) and age, gender and IQ matched healthy control (HC) children and adolescents (N = 43). All participants were female. The age of the participants ranged from 11–18 years of age. This sample size was based on a power calculation for detecting a medium sized effect with 80% power and a level of significant of 0.01.

AN participants were recruited from the Child and Adolescent Eating Disorder Service, South London and Maudsley NHS Trust. Most were receiving either outpatient treatment, or were attending a residential day programme. Two participants were receiving inpatient treatment. The inclusion criteria for the AN group included a DSM-5 diagnosis of Anorexia Nervosa and Ideal body weight (%IBW) of 90% or under. Percentage IBW shows what proportion of their optimal body weight an individual currently is, and it is corrected for age and gender [36].

Inclusion criteria for the HC group included a %IBW of 91% or above. Participants with a %IBW of 120 or over were excluded from the study. Participants were also excluded if they had a current or past history of an eating disorder or any other psychiatric disorder. This information was obtained during the SCID interview. Participants were also excluded if there was a current or past history of and ED in first or second degree relative. This information was collected with the demographic information. Exclusion criteria for both groups were a diagnosis autism spectrum disorder (ASD), psychosis, learning difficulty or being non-fluent in the English language. Within the AN group 85.4% were White British, and 81.4% of the HC group were White British.

All participants signed consent forms, and parental consent was also gained for each participant. This research was approved by a Research and Ethics Committee (REC no: 12/LO/2015).

Measures

Demographic measures. Percentage Ideal body weight (%IBW): A percentage of each participant's ideal body weight was calculated from measurements of their weight and height and corrected for age and gender [36].

The Structured Clinical Interview for DSM-IV Axis I disorders (SCID-I, [37]): Was used as a screening tool to assess the presence of possible psychiatric disorders in the AN and HC groups.

Neuropsychological measures. Intelligence Quotient (IQ): Weschler Abbreviated Scale of Intelligence (WASI [38]): The WASI is formed of the four subscales block design, vocabulary, matrix reasoning and similarities. Raw scores are calculated for each subscale and then scores are scaled by correcting for age. Scaled scores are then summed to give the verbal, performance and full scale IQ scores.

Set-shifting: The Wisconsin Card Sorting Test Computer version 4 (WCST[39]): Measure of set-shifting. Participants must match a number of stimulus cards to one of four category cards. Cards can be matched by colour, number or shape, and the rule must be worked out by trial and error based upon the feedback received. Once the participant has correctly matched the card for 10 consecutive sorts, the sorting rule changes and the participant must shift their response to work out the new sorting rule. The rule changes up to five times throughout the task, and every time a participant correctly completes a sort this is termed 'completing a set'.

The most commonly reported outcome from the WCST is the number of perseverative errors made by the participant. However, in order to mimic the largest dataset in adult AN [7], the current study will also report measures of general performance, perseveration, conceptual ability and response consistency. Further descriptions of each of these measures can be found in Tchanturia et al., 2012. The present study replicated the test parameters of Tchanturia et al., (2012), where by visual and audio feedback is given in a male voice one second after each sort has been made.

Central Coherence: The Rey-Osterrieth Complex Figure test (ROCFT[40]): A pen and paper task measuring global processing ability, participants are required to accurately copy a complex figure and the drawing strategy adopted by the participant is used as a measure of central coherence. The ROCFT is scored according to Booth's 2008 scoring method [6], which incorporates both the order in which the participant chooses to draw the elements (whether preference is shown to global or detailed elements) and the style in which they are drawn in (fragmented or coherently). Order index (OI) and style indexes (SI) are computed and are added to give the Central Coherence Index (CCI). For more details see Lopez et al., 2008 [41]. In order to check reliability, 15% of the entire sample was co-rated by a second rater. Inter-rater reliability was good with Cohens kappa = 0.71, $p = < .001$.

The Fragmented Pictures Task (FPT, [42]): A computerised task in which participants are presented with a picture that slowly develops frame-by-frame. Participants are asked to indicate verbally what the object is as quickly as possible. There is one practice trial followed by six test trials. The main outcome measure is the mean frame in which the participant correctly identifies the picture. The task is benefited from a global approach and quicker responses are indicative of better global processing [8, 42].

Self-report Questionnaire measures: Eating Disorder Examination Questionnaire (EDEQ [43]): A 36-item scale assessing eating disorder psychopathology. Clinical criteria cut-off adopted was a global score of higher than 2.7[44, 45]. Cronbach's Alpha for the current study was 0.98.

Hospital anxiety and depression scale (HADS [46]): Measures anxiety and depression symptomatology. The clinical cut off for this measure is 10. Cronbach's Alpha for the current study was 0.91.

Child Obsessive Compulsive Inventory (Choci [47]): Used to assess obsessive-compulsive symptomology in children and adolescents. The measure assesses both the content and the severity of the symptoms with a total score is calculated out of 40. Scores of 17 or above are suggested as a clinical threshold. Cronbach's Alpha for the current study was 0.94.

Autism-Quotient 10 (AQ-10, [48]): A shortened version of the Autism Quotient, used to assess autistic features and traits. The clinical cut-off is six or above. Cronbach's Alpha for the current study was 0.54.

The Detail and Flexibility questionnaire (DFLEX,[49]): The DFLEX is a 24-item scale assessing cognitive rigidity/detail focussed processing. Cronbach's Alpha for the current study was 0.80.

Procedure

Participant's height and weight data were collected on the morning of testing using SECA electronic scales, by a clinician as part of a treatment programme. Participants were asked to complete the self-report questionnaires and then the neuropsychological tasks were administered by a trained researcher (KL/SL).

Statistical analysis

Histograms were used to assess the data for normality. A number of the WCST outcomes were positively skewed (total response errors, perseverative responses, perseverative errors, non-perseverative errors, failure to maintain set). Standard log transformations were conducted to normalise the data. T-tests were used to test for differences in performance between the two groups on the transformed data. Log transformations were unable to normalise the learning to learn scale of the WCST, and so a Mann Whitney-U test was used. Due to the testing of multiple variables, we used a more conservative significance level of 1%, to minimise Type I errors.

The effect of confounding variables such as age and IQ were tested for and were non-significant and so these were not included in the final statistical model.

Correlations were used to examine associations between neuropsychological performance and clinical and demographic characteristics within the AN group. Cohen's d was calculated to provide effect sizes (<0.2 = small, <0.5 = medium, >0.8 = large). Data was analysed using the statistical package IBM SPSS version 21.00.

Results

Clinical and demographic data for the participants is displayed in Table 1.

IQ

There were no significant differences between the AN group and the HC group on any of the scales or subscales. However, there was a trend for higher performance in the AN group on the matrix reasoning sub-scale (see Table 2).

Neuropsychological outcomes: Set-shifting and central coherence

Fig 1 displays the z-scores for each group for the neuropsychological measures. Z-scores were calculated using the formula: (data point–healthy control mean)/healthy control SD, to depict the cognitive profile of the AN group against that of the HC group [5].

The figure suggests that there are no impairments in the AN group on any of the tasks (no scores fall below -1.5/-2), however the differences in processing style between the groups can be seen.

Wisconsin card sorting test. Table 3 displays the transformed and untransformed means and standard deviations for each of the WCST outcomes with p values and effects sizes.

Table 1. Participant demographics table (Means & SD).

	AN (N = 41)	HC (N = 43)	P value	Effect size (Cohen's d)
Age (years)	15.07 (1.81)	15.11 (1.94)	.93	-
%IBW	80.68 (6.57)	101.1 (8.41)	< .001(***)	-
BMI	16.16 (1.50)	20.34 (1.99)	< .001 (***)	-
Years of education	11.05 (2.00)	10.86 (1.90)	.77	-
Illness duration (Years)	1.70 (1.18)	-	-	-
Medication Use (%)	51.20	-	-	-
SSRI (%)	38.10	-	-	-
Olanzipine (%)	38.10	-	-	-
Both (%)	23.80	-	-	-
Age of onset (Years)	13.80 (2.30)	-	-	-
EDEQ Global	3.45 (1.79)	0.99 (0.70)	< .001(***)	1.85
AQ-10	3.90 (2.12)	2.67 (1.27)	< .01(**)	0.72
HADS Anxiety	12.34 (5.05)	4.72 (2.49)	< .001(***)	1.95
HADS Depression	7.93 (4.46)	2.09 (1.59)	< .001(***)	1.83
Choci	14.55 (13.11)	3.89 (5.32)	< .001(***)	1.09
DFlex Cog ridgidity	50.17 (14.62)	34.79 (7.40)	< .001(***)	1.35
DFlex Attention to detail	45.51 (14.62)	36.31 (7.89)	< .001(***)	0.80

Footnotes:

* Significant at 0.05

**0.01

***0.001

%IBW = %ideal body weight; BMI = body mass index (kg/m^2); EDEQ = Eating disorder examination questionnaire; AQ10 = Autism Quotient 10; HADS = Hospital anxiety and depression scale; DFlex = Detail and flexibility scale; Choci = Child Obsessive Compulsive Inventory.

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There were significantly more perseverative errors (p = < .01) and perseverative responses (p = < .01) made by the AN group, and there were trends towards significant differences in the number of categories completed (p = .03).

Rey-Osterrieth Complex Figure Test and Fragmented Pictures Task. Table 3 displays the means and standard deviations for each of the central coherence measures. The AN group

Table 2. Means (SD) and p-values for WASI.

	AN (N = 41)	HC (N = 43)	P value	Effect size (Cohen's d)
Verbal IQ	105.92 (21.30)	105.63 (11.26)	.94	0.02
Performance IQ	103.55 (14.00)	104.07 (11.81)	.86	0.04
Full Scale IQ	107.10 (13.76)	105.30 (10.29)	.50	0.15
Vocabulary	58.13 (10.02)	55.29 (8.23)	.23	0.31
Similarities	53.00 (16.12)	48.35 (6.34)	.14	0.39
Block design	56.31 (9.28)	52.32 (8.70)	.10	0.47
Matrix reasoning	56.31 (9.28)	51.94 (7.44)	< .05(*)	0.53

Footnotes:

* Significant at 0.05

**0.01

***0.001

IQ = Intelligence quotient

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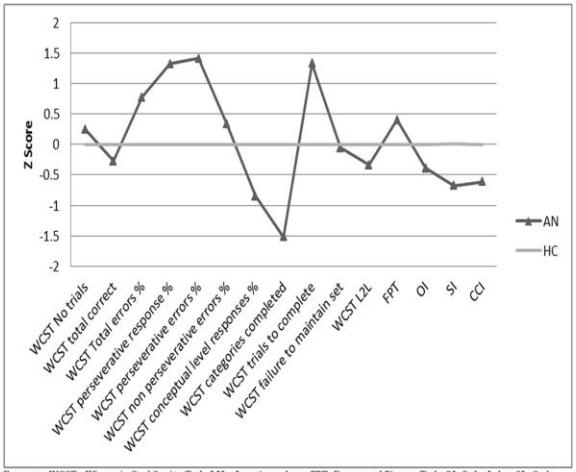

Footnotes: WCST= Wisconsin Card Sorting Task; L2L= Learning to learn; FPT=Fragmented Pictures Task; OI=Order Index; SI= Style Index; CCI=Central Coherence Index

Fig 1. Z scores for neuropsychological performance for AN and HC groups. Footnotes: WCST = Wisconsin Card Sorting Task; L2L = Learning to learn; FPT = Fragmented Pictures Task; OI = Order Index; SI = Style Index; CCI = Central Coherence Index.

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showed significantly lower scores on the style index ($p = < .01$) and the central coherence index ($p = < .01$) of the ROCFT. There was a trend for the AN group to show higher scores on the FPT ($p = .09$), indicating a more detail focussed approach.

Sub-analyses within the AN group

Medication analysis. To assess the impact of medication on neuropsychological processing the AN group was divided into two sub-groups 1) medication free and 2) on medication, and a t-test was used to assess any differences in neuropsychological processing between the two groups in perseverative errors in the WCST, ROCFT and FPT. There were no significant differences between the groups on any of the neuropsychological measures (WCST perseveration errors $p = .94$, Order Index $p = .88$, Style Index $p = .64$, CCI $p = .87$, FPT $p = .77$).

Associations with clinical and self-report measures. Correlations were used to test for associations between the neuropsychological performance measures (WCST perseveration errors, SI, OI, CCI and FPT) and clinical (%IBW, age of onset, length of illness) and self-report data (autistic traits, depression, anxiety and obsessive-compulsive traits). There were no associations between the WCST, OI, SI or CCI and the clinical or demographic variables. However there were some weak associations between the FPT and EDE-Q Global scale (.27, $p = .09$).

Discussion

This study aimed to investigate the neuropsychological processing profile of children and adolescents with AN. The findings suggest that they share a similar profile to adults with AN, with marked cognitive inefficiencies in set-shifting and central coherence relative to IQ. Firstly we found that there were no significant differences in any of the IQ scales or subscales of the WASI, with both groups exhibiting the same intelligence profile. Such findings are in accordance with previous studies of IQ in childhood AN, which also reported no differences in performance in comparison to HCs [50].

Regarding the neuropsychological measures we found that there were a significantly higher number of perseverative errors made by the AN group in the WCST, of medium effect size

Table 3. Set-shifting and central coherence outcomes: Means (SD) or medians (IQR), p-values and effect sizes.

Set-shifting outcomes: Wisconsin Card Sorting Test				
	AN (n = 41) Mean (SD)/ Median (IQR)	HC (n = 43) Mean (SD) Median (IQR)	P value	Effect size (Cohen's d)
General performance measures				
Number of trials administered	95.7 (20.2)	91.5 (17.1)	.28	0.23
Total correct responses	69.8 (11.1)	72.4 (9.5)	.62	0.00
Total response errors	26.2 (22.5)	18.3 (9.9)	-	
Total response errors %	18.0 (14.0–29.0)	18.5 (15.0–23.0)		
Total response errors% (transformed)	3.0 (0.5)	2.9 (0.3)	.25	0.25
Total categories completed	5.4 (1.4)	5.9 (0.3)	< .05(*)	0.51
Perseveration measures				
Perseverative responses	14.4 (15.1)	8.6 (4.6)	-	
Perseverative responses %	10.0 (8.0–15.5)	8.5 (7.0–10.3)		
Perseverative errors	13.1 (12.4)	8.1 (3.9)	-	
Perseverative errors %	10.0 (8.0–13.0)	8.0 (6.75–9.25)		
Perseverative errors% (transformed)	2.3 (0.5)	2.1 (0.3)	< .01(**)	0.49
Non-perseverative errors	13.2 (12.9)	10.2 (6.6)		
Non-perseverative errors %	9.0 (6.5–9.0)	10.0 (7.0–13.0)		
Non-perseverative errors% (transformed)	2.3 (0.7)	2.3 (0.5)	.81	0.00
Conceptual ability measures				
Trials to complete first category	16.8 (20.1)	12.5 (3.2)	.43	0.31
Conceptual level responses	63.3 (15.0)	68.7 (8.6)	.28	0.45
Conceptual level responses %	69.4 (20.5)	76.9 (8.9)	-	
Response Consistency measures				
Failure to maintain set	0.0 (0.0–1.0)	0.0 (0.0–1.0)	-	
Failure to maintain set (transformed)	0.9 (0.3)	0.9 (0.3)	.98	
Learning to learn	-1.26 (–2.7- –1.3)	-1.0 (–2.9- –1.0)	.26	
Central Coherence outcomes: Rey Osterrieth Complex Figure Test & Fragmented Pictures Task				
	AN (n = 41)	HC (n = 43)	Test statistic	Effect size (Cohen d-s)
FPT (Mean frame)	4.6 (0.7)	4.3 (0.6)	.09	0.38
ROCFT Order Index	1.5 (0.7)	1.8 (0.6)	.10	0.36
ROCFT Style Index	1.2 (0.5)	1.4 (0.4)	< .01(**)	0.62
ROCFT Central Coherence Index	1.0 (0.4)	1.3 (0.4)	< .01(**)	0.57

Footnotes:

* Significant at 0.05

**0.01

***0.001

IQR = Interquartile ranges; FPT = Fragmented Pictures Task; ROCFT = Rey Osterrieth Complex Figures Test.

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(d = 0.49). The AN group also exhibited lower style index and central coherence index scores on the ROCFT with medium effect sizes (d = 0.62 and 0.57 respectively). As can be seen from the Z-scores in Fig 1, the performance of the AN group in these task cannot be described as 'impaired', however, the AN group display a significantly different processing style to the HC group, characterised by subtle inefficiencies in both set-shifting and central coherence tasks. Overall, despite having similar IQ to the HC group, these results suggest an inflexible thinking style with poorer global integration in the AN group in young people. This is the first study to

demonstrate such inefficiencies in children and adolescents using the WCST and ROCFT, and mirror the effect sizes found in large experimental studies in the adult AN and HC females using the same tasks and same test parameters and scoring methods [7, 8]. However, it should be noted that unlike the results from adult AN studies [7], whereby there were differences between AN and HCs across all domains of the WCST, the present study only observed worse performance by the AN group in perseverative errors and perseverative responses. Such findings could suggest that domains other than perseveration could be more susceptible to the effects of starvation and chronicity of ED pathology, as theoretically the participants in adult AN studies are likely to have a longer duration of illness.

Secondary analyses within the AN group demonstrated that cognitive inefficiencies were independent of medication status and other clinical and demographic variables, such as % IBW, illness length or anxiety, depression and OCD symptomatology.

Systematic reviews and meta-analyses of set-shifting and central coherence in children and adolescents with AN found non-significant but worse performance within the AN group compared to HCs. It was highlighted that such non-significance could be due to small sample sizes and differences in methodology [32, 33]. The findings of the present study in part support this idea, as it had a large sample size, used robust neuropsychological tasks with the same test parameters of the adult studies and found significant differences between the AN and HC groups.

These findings add support to the possibility that the cognitive inefficiencies observed in this study are underlying traits. This is further supported by the fact the AN group were in the very early stages of illness. In studies with shorter durations of illness the effects of starvation or consequences of illness on cognitive processing should be less pronounced leaving underlying traits more visible. Although the presence of these characteristics may add support to the idea that they may be an endophenotypic trait for AN, they cannot confirm the hypothesis. Particularly as one recent study demonstrated that cognitive processing improved and was comparable to HCs, following weight restoration [51]. Further studies using long-term weight restored children and adolescents are required in order to confirm this.

Our findings carry important clinical and research implications. Firstly, the clarification that children and adolescents with AN do share the same cognitive processing inefficiencies as adults with AN has important implications for the treatment of AN. Although a large proportion of children and adolescents respond well to outpatient treatment (family therapy having the most efficacy [52]), there is still a significant amount of patients who do not appear to benefit from this treatment [53]. This suggests that the field needs to continue to develop effective treatments for the child and adolescent AN age group.

The observation of this specific neuropsychological profile in adults with AN lead to the development of Cognitive Remediation Therapy (CRT) for ED [54]. CRT is proving a popular and beneficial treatment for adults with AN, and there is emerging evidence demonstrating improvement to cognitive processing styles in adults [35]. There is already emerging evidence that young people find CRT a beneficial addition to treatment [55–57]; however it is most commonly used with the severe and enduring population to minimise discomfort. The evidence of a similar profile in adolescents strongly suggests that CRT could be a beneficial treatment for younger patients with AN, to help remediate inefficient cognitive processing.

Adding CRT to treatment protocols may be associated with improved outcomes for children and adolescents with AN, however, further randomised controlled trials of CRT with children and adolescents with AN are needed to confirm this.

Taken together with the findings of inefficient cognitive processing persisting following recovery and weight restoration in adults, this specific cognitive profile could be used to subtype AN from other eating disorders. Further work examining the neuropsychological profile

of other sub-types of eating disorders such as bulimia nervosa (BN) and binge eating disorder (BED) are needed.

The strengths of this study lie in its large sample size and the use of the same robust neuropsychological tasks that are used in the adult AN literature. A further strength is that it replicates the methodology used in the largest adult AN neuropsychological studies, allowing for comparisons with published data.

A methodological limitation of the present study is that pre-morbid weights were not reported. Therefore the degree of weight loss and the severity of starvation of each participant cannot be accounted for in the results. It is important for future studies to collect this data and account for it in the analyses.

Although this study's findings suggest underlying cognitive inefficiencies are present in children and adolescents with AN, it is important to acknowledge the typical developmental trajectory of both set-shifting and central coherence abilities. As discussed in a systematic review of set-shifting in children and adolescents with AN [32], previous research with healthy population samples has clarified that set-shifting abilities rapidly develop up to the age of eight years, with a moderate amount of development of these skills in early adolescence [58]. In terms of central coherence, there is a lack of developmental studies available, and it is suggested that central coherence can be viewed more as a processing style rather than an impairment or skill, and is based on a continuum from detailed-focussed to global integration [59]. The effects of starvation and malnutrition on the brain at such a critical developmental period should not be underestimated and should be considered when interpreting our results.

With this in mind, it will be important for future research in this area to use longitudinal designs and also to utilise neuroimaging to confirm whether the structural differences observed in adults samples are the same in younger populations. This will also help to identify the possible neural underpinnings of such inefficiencies.

The present study incorporated both the ROCFT and FPT to assess global processing. As performance on both of these tasks is benefitted from taking a more global approach, it would be beneficial for future studies to also use tasks where a detailed-focussed processing style is preferable, such as the group-embedded figures task [60]. This would allow us to confirm if children and adolescents with AN display weak central coherence (both a bias towards detail at the expense of the bigger picture), as is seen in the adult population [61].

To summarise, the present study has highlighted that children and adolescents with AN are likely to display a similar cognitive processing style to adults with AN, relative to IQ. These cognitive processing inefficiencies appear to be independent of clinical and demographic variables, suggesting that they could represent an underlying trait. Such findings carry important implications for the diagnosis and treatment of children and adolescents with AN.

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Author Contributions

Conceived and designed the experiments: KL KT. Performed the experiments: KL SL. Analyzed the data: KL MK. Contributed reagents/materials/analysis tools: KT. Wrote the paper: KL SL KT MS JT.

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CHAPTER 4

STUDY 2: IS INEFFICIENT COGNITIVE PROCESSING IN ANOREXIA NERVOSA A FAMILIAL TRAIT? A NEUROPSYCHOLOGICAL PILOT STUDY WITH UNAFFECTED MOTHERS OF OFFSPRING WITH ANOREXIA NERVOSA.

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4.1 Introduction

Anorexia Nervosa (AN) is an eating disorder (ED) characterised by distorted body image with excessive calorie restricting, leading to severe weight loss (American Psychiatric Association, 2013). Genetic studies have indicated high heritability rates, however thus far the search for the genes implicated in the development of AN has yielded disappointing results (Bulik et al., 2006). AN has one of the highest morbidity rates amongst psychiatric conditions, due to physical complications as well as high suicide rates (Arcelus et al., 2011). However despite this there is currently no recommended first-line treatment for adults with AN (NICE, 2004), and although family-based treatments are recommended for children and adolescents, there are still a significantly high number of non-responders to this treatment (Agras et al., 2004).

The combination of the ego syntonic nature of anorexia, limited insight and the high comorbidity rates observed within the disorder, often means that treating phenotypic behaviour is complicated and largely unsuccessful (Kaye et al., 2004; Konstantakopoulos, Tchanturia, Surguladze, & David, 2011). Therefore attention is now turning to investigating underlying mechanisms that may maintain the disorder and make it difficult to treat, such as possible inherited vulnerabilities or endophenotypic traits (Treasure, 2007). Elucidating these underlying markers can aid the understanding of the genetic vulnerabilities of AN, offering insights in to its biological underpinnings and uncover potential targets for treatments.

Inefficient cognitive processing, namely poor set shifting and global processing abilities, have been consistently reported in adults with AN (Lang, Lopez, Stahl, Tchanturia, & Treasure, 2014a; Roberts et al., 2007; Tchanturia et al., 2012b) This cognitive style is also present in an attenuated form in individuals who are weight-restored (Harrison et al., 2011; Roberts et al., 2010; Tchanturia et al., 2012b).

Until recently the data regarding the cognitive style of children and adolescents with AN was inconsistent (Andrés-Perpiña et al., 2011; Fitzpatrick, Darcy, Colborn, Gudorf, & Lock, 2012; Frampton, Hutchinson, Watkins, & Lask, 2012; Kjaersdam Telléus et al., 2014), with two recent meta-analyses acknowledging that methodological limitations were possibly contributing to these inconclusive results (Lang, Stahl, Espie, Treasure, & Tchanturia, 2014b; Lang & Tchanturia, 2014). A

recent study replicating the methodology of the adult AN studies provided strong evidence of inefficient cognitive processing within children and adolescents with AN (Lang et al., 2015b). Taken as a whole, the data from adult AN, adult recovered AN, and the more recent child and adolescent studies, have led to the thought that they could possibly represent an underlying trait for the disorder.

As these traits are common among numerous mental health conditions such as Obsessive Compulsive Disorder (OCD) (Head et al., 1989); Autism Spectrum Disorder (ASD) (Hill, 2004); and Schizophrenia (Pantelis et al., 1999), it is clear that they are important factors in the aetiology of complex psychiatric disorders.

Additionally, inefficient cognitive processing in AN appears to be familial as it is also present in unaffected family members (Galimberti et al., 2013; Roberts et al., 2010, 2013). Much of this work has compared discordant sister pairs to unaffected sister pairs, finding poor neuropsychological processing in unaffected sisters compared to HC sisters (Holliday, Tchanturia, Landau, Collier, & Treasure, 2005; Roberts et al., 2010). More recently, Galimberti et al. (2013) compared the performance on the Wisconsin Card Sorting Test (WCST) (Heaton, 1993), of AN mother and sisters to HC mothers and sisters, finding worse task performance in the AN proband. Roberts et al. (2013) also found weak central coherence to be present in unaffected sisters of those with AN. The results of these studies suggest that they are familial risk factors for AN, however studies of this design cannot distinguish between genetic and environmental factors and therefore inferences regarding the genetic influence of such characteristics cannot be made.

Preliminary results from the only available genetic study of cognitive processing in AN have highlighted the likely heritable nature of these characteristics by demonstrating a similar neuropsychological profile in both monozygotic and dizygotic twins (Kanakam et al., 2013). With this in mind, these findings have marked inefficient cognitive processing as a possible candidate for an endophenotype in AN.

A majority of familial studies in AN have focused on sister-pair designs, and to our knowledge central coherence in unaffected mothers of those with AN has not been studied yet. Investigating these well-established cognitive styles in AN in unaffected

mothers of offspring with AN is important because family interventions are widely used in the treatment of eating disorders, and better understanding of cognitive profiles in family members will help to innovate existing treatments and strengthen them (Galimberti et al., 2013).

Therefore the present study aimed to build on this knowledge further by specifically investigating the neuropsychological profile of unaffected mothers of offspring with a diagnosis of AN, and comparing their performance to healthy control (HC) mothers of healthy offspring. We wished to explore whether unaffected AN mothers would show an inefficient cognitive processing style in comparison to HC mothers.

4.2 Method

4.2.1 Participants

Participants included 21 unaffected AN mothers of children and adolescents with a diagnosis of AN, and 20 age, gender and IQ matched HC mothers of HC children and adolescents. The age of the participants ranged from 32-58 years. The unaffected AN mothers were a sub-sample of mothers of children and adolescents with a diagnosis of AN that had been recruited as part of a larger neuropsychological study (Lang et al., 2015b). The data from the offspring was analysed as part of the larger study and therefore is not reported here. However the results from the entire child sample can be found in (Lang et al., 2015b).

The inclusion criteria for the unaffected AN mothers group included having a daughter with a DSM-4 diagnosis of AN, and a Body Mass Index (BMI) of >18.5. Unaffected AN mothers were excluded if they had a current diagnosis or history of an eating disorder themselves. This was assessed during the SCID screening interview and a self-report questionnaire relating the eating disorder pathology.
Inclusion criteria for the HC mothers group was having a HC child taking part in the larger neuropsychological study, and having a BMI of >18.5.

HC mothers were excluded if they had a current or past history of an eating disorder or any other psychiatric disorder, or if there was a current or past history of and ED in a first or second degree relative. This was assessed through the use of the SCID screening interview, self-report measures and questions relating the family psychiatric history on a demographic questionnaire.

Exclusion criteria for both groups included a BMI of 30 or over, as there is evidence of inefficient cognitive processing in obese individuals (Wu et al., 2014).

Additional exclusion criteria for both groups included being non-fluent in the English language. All participants gave written consent. This research was approved by a Research and Ethics Committee (REC no: 12/LO/2015).

4.2.2 Measures

4.2.2.1 Demographic measures

Body Mass Index (BMI, kg/m2): Participants' heights and weights were measured and used to calculate their BMI.

The Structured Clinical Interview for DSM-IV Axis I disorders (SCID-I (First et al., 2012): was used as a screening tool to assess the presence of possible psychiatric disorders in the AN and HC groups.

4.2.2.2 Neuropsychological measures

Intelligence Quotient (IQ): Wechsler Abbreviated Scale of Intelligence (Wechsler & Hsiao-pin, 2011). The WASI is formed of the four subscales block design, vocabulary, matrix reasoning, and similarities. Raw scores are calculated for each subscale and then scores are scaled by correcting for age. Scaled scores are then summed to give the verbal, performance and full scale IQ scores. The WASI is well validated with established normative data (Wechsler & Hsiao-pin, 2011) and is known to have good psychometric properties, such as factor structure (Ryan et al., 2003) and construct validity (Canivez et al., 2009).

Set shifting:

The Wisconsin Card Sorting Test Computer version 4 (WCST (Heaton, 1993): Measure of set shifting. Participants must match a number of stimulus cards to one of four category cards. Cards can be matched by colour, number or shape, and the rule must be worked out by trial and error based upon the feedback received. Perseveration errors were used to measure set shifting abilities in this study.

Central Coherence:

The Rey-Osterrieth Complex Figure test (ROCFT, (Osterrieth, 1944): A pen and paper task measuring global processing ability, participants are required to accurately copy a complex figure and the drawing strategy adopted by the participant is used as

a measure of central coherence. The ROCFT is scored according to Booth's (2006) scoring method, giving an Order index (OI), style index (SI) and a Central Coherence Index (CCI) (Booth, 2006)). To check reliability 15% of ROCFT from the overall sample of the larger study (Lang et al., 2015b) were co-rated by a second rater. Inter-rater reliability was good, with Cohens kappa= 0.71, p=<.001.

The Fragmented Pictures Task (FPT, (Snodgrass et al., 1987): A computerized task in which participants are presented with a picture that slowly develops frame-by-frame. Participants are asked to indicate verbally what the object is as quickly as possible. There is one practice trial followed by six test trials. A mean frame in which the participant correctly identifies the picture is calculated, with lower scores indicating better global processing.

4.2.2.3 Self-report Questionnaire measures

Eating Disorder Examination Questionnaire (EDEQ, (Fairburn & Beglin, 1994): A 36-item scale assessing eating disorder psychopathology. Clinical criteria cut-off adopted was a global score of higher than 2.7. The EDE-Q has demonstrated good psychometric properties with high internal consistency (Peterson et al., 2007) and reliability (Berg et al., 2012). Cronbach's Alpha for the current study was 0.98.

Hospital anxiety and depression scale (HADS, (Zigmond & Snaith, 1983): widely used measure of anxiety and depression. The clinical cut off for this scale is 10. The HADS has shown to be a reliable measure of both symptom severity and caseness, as well as demonstrating good factor structure, discriminate and concurrent validity and internal consistency (Bjelland et al., 2002). Cronbach's Alpha for the current study was 0.90.

Obsessive Compulsive Inventory (OCI, (Foa et al., 2002)): Used to assess obsessive-compulsive symptoms. The OCI has been validated for use with both clinical and non-clinical groups, as well as showing good internal consistency in anxious and non-anxious groups (Abramowitz & Deacon, 2006; Foa et al., 2002). Cronbach's Alpha for the current study was 0.73.

Autism-Quotient 10 (AQ-10, (Allison et al., 2012)): A shortened version of the Autism Quotient, used to assess autistic features and traits. The clinical cut-off is six or above. The AQ-10 has shown to have good psychometric properties including good specificity, reliability and internal consistency (Allison et al., 2012). Cronbach's Alpha for the current study was 0.51.

The Detail and Flexibility questionnaire (DFLEX, (Roberts et al., 2011)): The DFLEX is a 24-item scale assessing cognitive rigidity/detail focused processing. The original paper for this measure reported high internal reliability and construct and discriminant validity (Roberts et al., 2011). Cronbach's Alpha for the current study was 0.91.

4.2.3 Procedure

Participants' height and weight data were collected on the day of testing. Participants completed the self-report questionnaires and then the neuropsychological battery was administered by a trained researcher (KL). AN and HC offspring also had taken part in the same test procedure.

4.2.4 Statistical analysis

Histograms were used to assess the data for normality. The percentage perseverative errors scores of the WCST were positively skewed and standard log transformations were conducted to normalize the data. T-tests were used to test for differences in performance between the two groups on the transformed and untransformed data.

Correlations were used to examine associations between neuropsychological performance and clinical and demographic characteristics within the AN group.
Bonferroni corrections were applied to correct for multiple comparisons and the significance level was lowered to p=0.01.

Cohen's d was calculated to provide effect sizes (<0.2 = small, <0.5 = medium, >0.8 = large). Data was analysed using the statistical package IBM SPSS version 21.00.

4.3 Results

Clinical and demographic data for the participants is displayed in table 1. The groups did not significantly differ on any of the measures apart from self-reported depression and anxiety, where the unaffected AN mothers had significantly higher scores.

	Unaffected AN mothers (N=21)	HC mothers (N=20)	P value
Age (years)	48.90 (4.05)	47.75 (5.48)	.455
BMI	23.46 (3.16)	24.27 (2.27)	.368
Years of education	15.05 (3.5)	16.20 (2.14)	.203
Ethnicity (%WB)	90.00	89.50	
VIQ	103.56 (10.93)	100.12 (10.33)	.359
PIQ	103.44 (14.88)	111.00 (18.32)	.204
FSIQ	104.45 (11.61)	104.84 (11.70)	.917
EDEQ Global	0.72 (0.87)	0.87 (0.72)	.568
AQ-10	1.81 (1.54)	1.82 (1.65)	.976
HADS Anxiety	8.05 (5.13)	4.79 (1.81)	.011
HADS Depression	4.66 (3.37)	2.68 (2.31)	.035
OCI-R	9.33 (7.30)	9.68 (5.4)	.874
DFlex Cog rigidity	32.76 (9.63)	36.80 (6.92)	.133
DFlex Attention to detail	28.33 (9.82)	33.00 (7.74)	.106
SAS	9.90 (6.78)	7.96 (4.14)	.287
WASAS	3.00 (9.15)	1.72 (3.01)	.575

BMI=Body Mass Index (kg/m2); %WB= Percentage White British.; VIQ=Verbal IQ; PIQ=Performance IQ; FSIQ=Full scale IQ; EDEQ Global= Eating Disorder Examination Questionnaire Global Scale; AQ-10= Autism Quotient 10; HADS=Hospital Anxiety and Depression Scale; OCI-R= Obsessive-Compulsive Inventory-Revised; DFlex= Detail and Flexibility; SAS= Social Anhedonia Scale; WASAS= Work and Social Adjustment Scale.

Table 1 : Participant demographics for unaffected mothers and HC mothers.

4.3.1 Neuropsychological performance

Table 2 displays the means and standard deviations for each of the neuropsychological outcomes.

T-tests revealed that the unaffected AN mothers displayed significantly more perseverative errors (p=<.01) in comparison to the HC mothers. The unaffected AN mothers group displayed a significantly higher mean score on the FPT (p=.01), as well as significantly lower OI (p=.01), SI (p=<.01). There was a trend towards significance on the CCI (p=<0.05), with unaffected AN mothers scoring lower.

	Unaffected AN mothers (N=21)	HC mothers (N=20)	P value	Cohen's *d*
WCST perseverative errors (transformed)	2.5 (0.60)	2.10 (0.39)	<0.01	0.81
FPT mean frame	5.16 (0.64)	4.60 (0.67)	<0.01	0.88
ROCFT Order Index	1.64 (0.76)	2.16 (0.50)	<0.01	0.82
ROCFT Style Index	1.18 (0.54)	1.60 (0.41)	<0.01	0.90
ROCFT CCI	1.25 (0.42)	1.50 (0.29)	<0.05	0.71

WCST= Wisconsin Card Sorting Test; FPT= Fragmented Pictures Task; ROCFT= Rey Osterrieth Complex Figures Test; CCI= Central Coherence Index

Table 2: Neuropsychological outcomes of unaffected AN mothers and HC mothers.

4.3.2 Sub-analysis within the unaffected mother group

Associations with clinical and self-report measures:

Pearson's correlations were used to assess the associations between the neuropsychological outcomes and the self-report measures in the unaffected AN mothers group. There were trends toward a significant positive association between the amount of perseverative errors on the WCST and self-reported anxiety (.425, p=<.05), and a significant negative association between the FPT and obsessive-compulsive symptomatology (-.518, p=<.05).

4.4 Discussion

This study aimed to investigate the familial nature of set shifting and central coherence in unaffected AN mothers of offspring with AN. One set shifting (WCST) and two central coherence tasks (FPT, ROCFT) were administered to both groups. Their offspring had previously taken part in the larger study with the same tasks, and had demonstrated inefficient set shifting and low levels of global processing (Lang et al., 2015b)

We found unaffected AN mothers displayed a more inflexible thinking style as evidenced by a higher number of perseverative errors on the WCST, compared to HC mothers. Lower levels of global processing were also observed in the unaffected AN mothers group. Once multiple comparisons were corrected for, there was a trend towards significant group differences on the CCI scale of the ROCFT; however, this could be due to lack of power. Significantly lower levels of holistic processing were observed on the FPT and the order and style index of the ROCFT. This is the first study to our knowledge to specifically investigate these cognitive features, particularly central coherence, solely in unaffected mothers of offspring with AN. This study adds to the findings of other studies using numerous neuropsychological tasks showing consistent evidence of inefficient set shifting and weak central coherence associated with AN (Lang et al., 2014a; Roberts et al., 2007; Wu et al., 2014).

Taken together with previous findings, the present results add further support to the notion that inefficient cognitive processing is a familial trait in AN, occurring at a higher rate within unaffected first-degree relatives of those with AN, than in the healthy population.

It is important to note that in the present study, there were no significant differences between the mother groups in BMI or self-reported eating disorder, obsessive-compulsive pathology or autistic traits. However, there were significant differences in self-reported anxiety and depression. The raised levels of anxiety and depression in the unaffected AN mothers group are not surprising given that caring for a loved one with an ED is associated with significant stress and burden (Graap et al., 2008).

The elevated anxiety levels were approaching being significantly associated with a more inflexible thinking style in the unaffected AN mothers. There is literature to suggest that cognitive inflexibility is associated with a range of psychiatric disorders. Therefore higher levels of psychopathology in the unaffected AN mothers group could in part explain the group differences. However, as associations between anxiety levels and performance on the WCST were approaching significance, this is unlikely to account for the differences in performance.

The results of this study further highlight the important role that inefficient cognitive processing is likely to play as both an inherited vulnerability and a maintaining factor in AN. The unhelpful cognitive style observed in individuals with AN is placed as a core maintaining factor by numerous prominent models of AN (Connan et al., 2003; Southgate et al., 2005; Treasure & Schmidt, 2013). High levels of cognitive inflexibility and excessive detail focus within families caring for an individual with AN could further maintain the disorder by promoting maladaptive responses and behaviours that inadvertently serve to accommodate and sustain the eating disorder.

The role that these familial traits may possibly play in the maintenance of AN may suggest that it would be beneficial for family members to participate in cognitive remediation programmes with their affected relatives (Hutchison, Roberts, & Lask, 2014). The findings of an exploratory study suggested that involving family members in Cognitive Remediation Therapy (CRT) was beneficial for both patients and carers (Lang, Treasure, & Tchanturia, 2014c).

The results for the present study provide further support for this approach, and could possibly lead to improved outcomes for AN overall.

Although inefficient set shifting has been identified in numerous complex psychiatric disorders, such as OCD (Head et al., 1989), schizophrenia (Pantelis et al., 1999) and ASD (Hill, 2004), evidence of its familial vulnerability in some of these disorders is inconsistent. Some studies of unaffected relatives in OCD have shown poor set shifting whereas others have not (Cavedini, Zorzi, Piccinni, Cavallini, & Bellodi, 2010; Delorme et al., 2007). Similarly a meta-analysis in unaffected relatives in schizophrenia showed effect sizes ranging between .2-.4 when looking at the WCST

(Snitz, MacDonald, & Carter, 2006). For AN the pattern of heritability seems stronger, with different first degree relatives consistently showing inefficient cognitive processing on a number of neuropsychological measures with medium to large effect sizes (Galimberti et al., 2013; Holliday et al., 2005; Roberts et al., 2010). This data further supports the idea that these characteristics represent a vulnerability marker for AN within families.

Although it is acknowledged that genetic and environmental effects cannot be distinguished in the present studies design, when taken together with tentative results from early genetic studies they suggest that they are an inherited vulnerability in AN and could possibly represent an endophenotypic trait in AN. Elucidating potential underlying traits could be important for our understanding of the aetiology of AN by aiding our understanding of the genetic vulnerability of AN and uncovering potential targets for candidate genetic studies.

However, whilst the results from this and other familial studies highlight the inherited risk of inefficient cognitive processing within AN, this data alone cannot be used to confirm the notion that they may represent an endophenotype.

In order to qualify as an endophenotypic trait the characteristic must demonstrate its independence from the illness state (Gottesman & Gould, 2003). This is yet to be truly demonstrated within the AN literature, and therefore it is an important step for future studies to examine cognitive processing longitudinally, once weight has been restored and is stable. Shared environmental factors within AN families that are unaccounted for in the present study, may have also contributed to these similarities in cognitive style within families. Without a measure of cognitive functioning within families prior to illness onset we cannot be certain of whether genetic or environmental factors, or indeed an interaction between the two, are attributable to this outcome. Future studies should therefore seek to elucidate these factors. The findings of such studies could also have important implications for our understanding of maternal cognitive style as a risk factor for AN in offspring.

Amongst this study's limitations are its small sample size. As differences were detected between the groups, it suggests that the study does not lack power, however further replication of this study with larger sample sizes is desirable.

Secondly, it did not employ a measure of central coherence that is favoured by a detailed-focused approach, for example the Group Embedded Figures Test (GEFT). Weak Central Coherence (WCC, a processing bias toward details at the expense of holistic processing) has been identified in adults with AN (Lang et al., 2014a),. However we cannot conclude that unaffected parents display WCC, only poor global processing. Future studies may wish to examine this.

Future studies may also incorporate neuroimaging (such as functional magnetic Resonance Imaging, fMRI) with neuropsychological studies with unaffected relatives to elucidate possible neurocorrelates of inefficient cognitive processing. Neuroimaging studies have revealed differential brain activation in AN when performing both set shifting and central coherence tasks (Fonville et al., 2013; Garrett et al., 2014; Lao-Kaim et al., 2015; Zastrow et al., 2009), suggesting that different brain networks may be involved in cognitive processing in AN. Data from imaging studies with unaffected relatives who do not exhibit eating disorder pathology and therefore should not demonstrate neurological scars of starvation, could allow us to investigate the biological substrates involved in these neurocognitive characteristics further.

4.5 Conclusion

In summary, findings from the present study support that inefficient cognitive processing may be a familial trait in AN, and in combination with the results of preliminary genetic studies, may add further evidence to support the notion that it may represent an endophenotypic trait. This finding carries important clinical implications for the disorder regarding possible treatment options involving carers, as well as identifying genetic candidates for AN. However, longitudinal data from weight-restored individuals are needed to support the endophenotype hypothesis.

CHAPTER 5

STUDY 3: ACCEPTABILITY AND FEASIBILITY OF SELF-HELP COGNITIVE REMEDIATION THERAPY FOR ANOREXIA NERVOSA DELIVERED IN COLLABORATION WITH CARERS: A QUALITATIVE PRELIMINARY EVALUATION STUDY

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Acceptability and feasibility of self-help Cognitive Remediation Therapy For Anorexia Nervosa delivered in collaboration with carers: A qualitative preliminary evaluation study

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ABSTRACT

Anorexia nervosa (AN) is an eating disorder without a recommended first-line treatment. Cognitive Remediation Therapy (CRT) is showing great promise in helping patients reduce cognitive inflexibility and excessive detail focus, thinking styles that could make engaging in psychological therapies difficult. CRT has shown to be effective, feasible and acceptable in both individual and group formats, and positive qualitative data has been gathered from both service users and clinicians. The aim of the current study was to assess the use of CRT as a self-help treatment for individuals with AN delivered in collaboration with carers. Six families underwent a six-week self-help CRT intervention. Feedback was gathered from qualitative interviews and analysed using thematic analysis. Neuropsychological outcomes were also collected. Participant feedback regarding the intervention was generally positive, with participants describing a number of benefits such as it creating a space for families to spend time together outside of the eating disorder, acting as a 'gateway' for more emotional work and helping participants to gain insight into their cognitive profiles. These preliminary findings suggest that self-help CRT delivered in collaboration with carers is an acceptable form of treatment, and adds to the growing literature supporting CRT for AN.

1. Introduction

Anorexia nervosa (AN) is an eating disorder characterised by persistent restriction of calorie intake, a fear of gaining weight and a disturbance in body perception (DSM-5, APA, 2013). AN carries one of the highest morbidity rates amongst mental health disorders (Arcelus et al., 2011), and is associated with significant carer stress and burden (Treasure et al., 2003; Graap et al., 2008). Despite this, there is currently no established first-line treatment for AN (Bulik et al., 2007). One reason psychological treatments may be less than optimal for this disorder could be due to inefficient information-processing systems that have been observed within this population (Treasure and Schmidt, 2013). Both clinical observations and robust experimental evidence have identified a certain neuropsychological profile marked by inefficient set shifting (i.e., cognitive inflexibility) and weak central coherence (i.e., poor global processing with excessive bias towards detail) in adults with AN (e.g. Tchanturia et al., 2012a; Lang et al., 2014a). The data regarding the neuropsychological profile of children and adolescents with the disorder have thus far has been inconsistent (Lang et al., 2013; Lang and Tchanturia, 2014b). Some studies have demonstrated worse performance by children with AN compared to healthy controls on neuropsychological tasks (McAnarney et al., 2012; Andres-Perpina et al., 2011), whereas some have shown comparable performances (Sarrar et al., 2011; Rose et al., 2014). There is also evidence of a genetic component, as inefficient cognitive processing has also been shown to be present in unaffected sisters of those with AN (Holliday et al., 2005; Roberts et al., 2010) as well as some preliminary evidence of their presence in unaffected parents. Goddard reported that mothers with offspring with EDs demonstrated a strong bias toward detail-focussed processing coupled with poor global integration, as well as showing lower levels of cognitive flexibility in comparison to mothers of healthy offspring (Goddard, unpublished Ph.D. thesis). These experimental observations within the adult AN literature have been translated back into clinical practice and as a consequence, Cognitive Remediation Therapy for AN (CRT) has been developed to tackle these underlying mechanisms (Tchanturia,

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2014a; Tchanturia et al., 2013), and is showing great potential as an effective and highly acceptable treatment. CRT targets thinking styles seen in AN, such as cognitive inflexibility and excessive focus on detail, without discussions about eating disorder symptom-related issues. It uses cognitive exercises to encourage a more flexible thinking style, as well as bigger picture thinking. Randomised controlled trials indicate improvements in cognitive processing post-intervention (Brockmeyer et al., 2014; Dingemans et al., 2014; Lock et al., 2013; for reviews, Tchanturia et al., 2014b; Dahlgren and Rø, 2014) and group CRT is also well received (Genders and Tchanturia, 2010; Pretorius et al., 2012). There is also positive preliminary evidence of its benefit with children and adolescents with AN (Wood et al., 2011; Pretorius et al., 2012; Dahlgren et al., 2013). In addition to improvements in neuropsychological function, important information regarding individual's experiences of the treatment has also been sought.

Qualitative analyses of patients' and therapists' end of therapy letters demonstrate that both parties feel positive about CRT, acknowledging improvements in motivation and neuropsychological function (Whitney et al., 2008; Easter and Tchanturia, 2011). In addition, qualitative feedback has demonstrated that clinicians feel that CRT is a powerful engagement tool that can be used to work with patients in a light-hearted and fun manner (Lounes and Tchanturia, 2014).

CRT's potential in individual and group formats, combined with the positive feedback received from both patients and clinicians suggest that it could be important to develop this resource further in the context of a family intervention (Lask, 2014). Another potential avenue that remains unexplored is the extension of CRT for AN to a self-help format. Cost effective treatment modalities, such as self-help, that can increase accessibility to services for patients as well as reducing costs relating to clinician input are very attractive in today's health service. Similarly, it is of increasing value to involve family and carers more in treatments for AN, as reducing carer stress and burden levels can lead to better coping abilities and ultimately lead to better treatment outcomes (Goddard et al., 2011).

The aim of the current study was therefore to assess the feasibility and acceptability of CRT through a self-help format to be delivered in collaboration with carers. This was evaluated through a pilot study using both qualitative and experimental measures.

2. Methods

2.1. Participants

A sample of 12 participants took part in the study, including six females with AN and six mothers. Participants were recruited from advertisements placed on the eating disorder charity Beat website, support groups and the Child and Adolescent Eating Disorder Service at the South London and Maudsley Trust hospital. The inclusion criteria for the study were as follows: (i) Both an offspring with a diagnosis of Anorexia Nervosa or EDNOS-AN (in-line with DSM-IV) and their mother were willing to participate; (ii) offspring was aged between 12 and 40 years of age. Exclusion criteria for the study included (i) brain injury, (ii) mother was unable to participate; (iii) insufficient English language. Written and informed consent was obtained from all participants, and the study was approved by the Dulwich Research and Ethics Committee (study number 12/LO/2015). The ages of the AN participants ranged from 14 to 32 years (S.D.=6.78), (see Table 1 for participant characteristics). Four participants were adolescents (14–18 years). The ages of the mothers ranged from 45 to 64 years. One of the mothers had a history of an eating disorder.

2.2. Materials

2.2.1. Treatment

2.2.1.1. CRT manual. Participants were each given a copy of the CRT self-help manual. The self-help CRT manual was adapted from the original clinician manual

Table 1
Participant demographics and pre and post-intervention questionnaire data.

Group	Age	BMI	Pre					Post				
			EDE-Q global	HADS	DFlex		WASAS	EDE-Q global	HADS	DFlex		WASAS
					Cognitive rigidity	Attention-detail				Cognitive rigidity	Attention-detail	
AN	19.52 (14.00–32.50) (6.78)	17.10 (1.70)	3.43 (1.43)	25.25 (7.41)	81.00 (34.27)	60.50 (11.62)	22.25 (14.66)	2.40 (0.79)	19.75 (3.59)	64.20 (38.89)	51.00 (13.65)	14.31
Mothers	53.80 (45.11–64.40) (7.28)	23.95 (2.46)	1.23 (1.01)	10.20 (7.85)	31.6 (6.88)	35.40 (22.03)	1.60 (4.00)	0.731 (0.42)	9.00 (5.29)	30.25 (4.71)	25.75 (13.50)	0.67 (1.15)

BMI: Body Mass Index; EDE-Q global=Eating Disorder Examination Questionnaire Global score; HADS=Hospital Anxiety and Depression scale; DFlex=Detail and flexibility questionnaire; WASAS=Work and Social Adjustment Scale.

(Tchanturia et al., 2010; www.katetchanturia.com). It contained an introduction explaining the rationale of CRT, CRT tasks targeting cognitive inflexibility and bigger picture thinking and finally, a 'frequently asked questions' section. Feedback from a previous focus group had suggested that some tasks were too difficult to carry out in a self-help format and so were removed from the manual. The feedback had also suggested that reflecting on tasks had been difficult, so a 'tips for reflecting' section was also added to the manual. A copy of the amended manual can be found at www.katetchanturia.com. The parent's role in the intervention was to participate in the tasks with their offspring over the 6-week intervention.

2.2.1.2. CRT diary. Participants were also given a CRT diary and asked to make a record of every time they did a CRT task. They were asked to record what they did, who was involved and how long they spent on the given tasks.

2.2.2. Assessment

2.2.2.1. Interview schedule. A semi-structured interview schedule was developed for the study for use with both individuals with AN and their mothers. It contained questions assessing expectations prior to treatment, pros and cons of the treatment being delivered in a self-help format and pros and cons of working with family members. A copy of the interview schedule can be found in the Appendix A.

2.2.3. Neuropsychological measures

The Wisconsin Card Sorting Task (*WCST*, Heaton et al., 1993): The WCST is a computerised task used to assess set shifting abilities. Participants are presented with a stimulus card and are required to match it to one of four category cards (1 red triangle, 2 green stars, 3 yellow crosses or 4 blue circles). The correct way to sort the cards is unknown and the participant must use feedback on whether they have sorted correctly to guide their next move. The sorting rule changes unpredictably and the participants must adapt to the rule change. The number of perseverative errors is used as a measure of set shifting. A perseverative error is a particular error by which the participant continues to use the old (and now redundant) sorting rule.

The Rey Osterrieth Complex Figures Test (*ROCFT*, Osterrieth, 1944): The ROCFT is a pencil and paper task used to assess central coherence. Participants are asked to copy a complex shape. The drawing style adopted by the individual is used to measure central coherence abilities. The Booth (2006) method of scoring was used whereby order, style and central coherence indices are calculated. The order index is calculated from the first six elements drawn (higher scores are awarded when preference is shown to more global elements). The style index however is calculated by scoring six components of the ROCFT for the "degree of continuity in the drawing processes" (Booth, 2006). The central coherence index is obtained by summing the order and style indices. Performance on the ROCFT is benefited by a global approach. A second researcher who was independent of the study, co-rated 50% of the ROCFTs. Inter-rater reliability was very good (kappa=0.80).

2.2.4. Self-report measures

The Eating Disorder Examination Questionnaire (*EDE-Q*, Fairburn and Beglin, 1994): The EDE-Q is a measure of eating disorder psychopathology and contains 36-items scored on a 7-point likert scale. The EDE-Q contains four sub-scales (restraint, weight concerns, shape concerns and eating concern) from which a global score is calculated. The total score of each sub-scale is 6, with higher scores indicating more severity. It is widely used and is the gold standard measure in the eating disorder literature. Internal consistency in the current sample was excellent with Cronbach's alpha coefficients ranging between 0.91 and 0.98.

The Hospital Anxiety and Depression Scale (*HADS*-Zigmond and Snaith, 1983): Self report measure of anxiety and depression symptomatology. The measure gives separate subscale measures for anxiety and depression (7 items each) as well as a total score. The clinical cut off for this measure is 10. It is known to have good psychometric properties, with excellent internal consistency being demonstrated in the current sample with Cronbach's alpha coefficients ranging between 0.91 and 0.98.

The Detail and Flexibility Questionnaire (*DFLEX*, Roberts et al., 2011): The DFLEX is a 24-item scale tapping into both flexibility (e.g. *'When others suggest a new way of doing things, I get upset or unsettled'*) and bigger picture thinking (*e.g. 'I can get hung up on details when reading rather than understanding the gist'*). Answers are given on a 6-point likert scale. The 12 odd items of the measures are added to calculate a cognitive rigidity subscale and 12 even numbers are added to generate the detail focus sub-scale. The DFLEX has good psychometric properties, and in the current sample good-excellent internal consistency was demonstrated with Cronbach's alpha coefficients ranging between 0.79 and 0.90.

Work and Social Adjustment Scale (*WSAS*, Mundt et al., 2002): AN is associated with severe impairments (Tchanturia et al., 2012b). This was measured using the WSAS, a five-item measure of impairment in daily functioning, which has proven reliability and validity. Scores are rated on a 9-point likert scale with higher scores indicating increased impairment in functioning. The clinical cut offs for this measure are: 0–10 Subclinical, 10–20 significant functional impairment, >20 moderately severe. Internal consistency in the current sample was excellent with Cronbach's alpha coefficients ranging between 0.95 and 0.99.

2.3. Procedure

2.3.1. Training

A 2-hour training session was provided for the participants and their mothers and led by two of the authors (KT and KL). It should be noted that although in some cases fathers did take part in the treatment phase of the study, only mothers attended to initial training sessions and follow-up focus group. Therefore only data from participants and their mothers are presented here. The training session included a brief introduction about the rationale and principles of CRT for AN, suggestions on how to use it in everyday life and role-plays of CRT tasks. Participants were also asked to complete neuropsychological measures of set shifting and central coherence along with the aforementioned self-report measures at this session.

2.3.2. The intervention

Participants underwent a 6-week intervention period, wherein they used the manual in a collaborative fashion, but without the input of a therapist. Both participants and mothers were instructed that the treatment should be a collaborative process, whereby both parties should take part in the tasks. Participants were instructed to work through the manual at their own pace, but as a guide 20 min of CRT exercises twice a week were suggested. They were given the researchers' contact details (KL) in the event of having questions regarding the manual or CRT delivery. Participants were asked to keep a diary during the 6 weeks, recording when they did CRT, and for what time period.

After the 6-week intervention period, participants were invited to a focus group session during which a semi-structured interview was administered to obtain qualitative data. If participants were unable to come to the focus group then individual telephone interviews were arranged. The main focus group interview was 52 min and 4 seconds long. The interview conducted over the telephone with one family was 17 min and 19 s long. All interviews were audio-recorded using a Dictaphone.

Follow-up neuropsychological and self-report data were also collected during the feedback sessions.

2.4. Analysis of transcripts

Transcripts were typed up verbatim. The data collected from the telephone interview were added to the data collected from the focus group. Participants were sent copies of their transcripts to verify the content. The transcripts were analysed using thematic analysis (Joffe and Yardley, 2004; Braun and Clarke, 2006). One coder (KL) initially read through the transcripts and coded for certain categories. If a category was mentioned more than once they were then made into broader semantic themes. For example if the convenience of being able to carry out CRT in their own time was mentioned more than once, this was then made into the broader theme of 'acceptability of the treatment'.

A second coder who was independent of the research was then asked to read the transcripts and qualify the themes. They were asked to modify or add any themes they felt had been missed. Both researchers showed agreement, indicating good reliability and consistency of the themes.

3. Results

One AN participant did not complete the intervention stage of the study as they were admitted to an inpatient unit for treatment; it was therefore not possible to conduct the outcome measures. One family was not able to attend a focus group in person, so interviews were conducted over the phone. Overall five participants and five mothers completed the intervention and qualitative interview and follow-up self-report measures, with four of these families completing the post-intervention neuropsychological tasks.

3.1. Neuropsychological measures

Table 2 displays the pre- and post-scores for neuropsychological measures of set shifting and central coherence for each AN participant and mother. Visual inspection shows that the scores on both the WCST

Table 2
Pre and post-neuropsychological outcome data.

Group	Pre-intervention					Post-intervention				
	WCST perseverative errors (%)	WCST total error score	Order index	ROCFT style index	CCI	WCST perseverative errors (%)	WCST total error score	Order index	ROCFT style index	CCI
AN mean (S.D.)	12.00 (8.86)	22.50 (17.06)	1.44 (0.34)	1.31 (0.59)	1.16 (0.44)	6.75 (3.40)	10.50 (5.92)	1.95 (0.52)	1.53 (0.40)	1.38 (0.27)
						$d=0.8$	$d=0.96$	$d=0.21$	$d=0.47$	$d=0.64$
Parent mean (S.D.)	10.00 (3.22)	20.67 (6.77)	1.64 (0.83)	1.38 (0.37)	1.20 (0.40)	9.00 (2.94)	21.00 (6.06)	2.30 (0.25)	1.75 (0.29)	1.61 (0.21)
						$d=0.36$	$d=0.06$	$d=1.1$	$d=1.21$	$d=1.34$

WCST=Wisconsin Card Sorting Task; ROCFT=Rey Osterrieth Complex Figures Test; CCI=Central coherence index.

Table 3
Weekly times spend on CRT tasks as reported in CRT diaries.

Week	Mean time spent (minutes)
1	18.33
2	20.00
3	15.00
4	12.07
5	19.17
6	16.23

and the ROCFT were improved for AN participants post-treatment. Similarly, scores also improved in the parent group.

3.2. CRT diary

Table 3 displays the average amount of times that the families reported spending on the CRT tasks each week in the CRT diaries.

3.3. Qualitative analysis

Table 4 displays the main themes and sub-themes.

3.4. Acceptability of CRT as a self-help treatment

The participants were asked a number of questions to help assess whether they felt CRT could be delivered in this modality. The following themes arose from these discussions.

3.5. Convenience

All of the participants and mothers felt that the self-help format had been a convenient way to deliver this treatment:

Participant 4: "*It could be a bit more spontaneous as well because you didn't have a set time to do it. I mean we tended to do it around meal times so that I ate and I would do it to kind of take my mind off of it and that was helpful I think.*"

Mother 1: "*…the fact that you could spend a short time or a long amount of time…[made it]… very flexible, and I enjoyed it, it was great fun. […] However deeply you want to go with it is up to you.*"

Mother 6: "*… I kind of thought it would be longer, more difficult and the exercises would be more time consuming, that kind of thing… I think [this] was a positive because it made it easy […] to get on with it at home.*"

3.6. Reflecting on CRT tasks without a therapist

Some of the AN participants reported that there had been times when they had tried CRT tasks on their own without a parent. Three AN participants commented that being left to reflect on their thinking styles alone had been difficult. The main reason why this appeared to be difficult seemed to be due to a tendency to avoid going beyond one's comfort zone.

Participant 1: *"I think had I done it totally on my own, without mum I probably wouldn't have totally engaged with doing the reflective bits."*

Participant 1: *"Although I felt having to do the reflections… the questions afterwards was like doing therapy […]it was like 'oh this is a fun task', now ask me a question about how it related to life, 'oh now I'm crying'"… RESEARCHER: "So the reflecting bit was hard?" Participant 1: "Yes".*

Participant 6: *"Yeah that was also hard, I had to go back and do it again and think about what I was doing"*

3.7. Time constraints

One mother felt it was difficult to find the time to do it at home:

Mother 3: *"It was just hard to find the time, it was because I felt the onus was on me, and so I had to, so I'd say 'oh let's do it now', she'd go 'oh not now, let's do it in a bit', and then of course a bit later then I'd forget or be doing something else…"*

3.8. Acceptability of CRT with family members

A number of questions were also focused on discussing the positives and negatives of working collaboratively as a family on the self-help manual. The following themes arose:

3.8.1. Equality/putting child and parent on a 'level playing field'

All of the participants with AN and one mother felt that one of the benefits of working in collaboration with a family member was that it put them on a 'level playing field'. They suggested that working together on the manual and reflecting on their own thinking styles allowed them to feel equal to one another, and not as though the parent was leading the child through therapy.

Participant 1: *"Suddenly we're on kind of an equal relationship and I had to listen to her answers as well and stuff. This is just usually about me."*

Participant 4: *"With you doing it together, it did put you on equal ground almost, so it wasn't you just being asked loads of questions and someone prodding you. […] mum would go 'oh how could you*

Table 4
Main themes and sub-themes.

1. Acceptability of Self-help CRT	+ Convenient – Difficult reflecting without a therapist – Time constraints/prioritising
2. Acceptability of family involvement in CRT	+ Putting family members on equal playing fields + Spending 'fun' time together outside of the eating disorder + Family can help with reflections + 'Stepping stone' for more difficult and emotional conversations + Can help with familial cognitive profile – Child not always responsive to parent 'pushing'
3. Raising awareness/insight into neuropsychological profile	+ Awareness into cognitive profile can help build confidence to start to make changes + Generalise to real-life setting
4. Real-life applications/positive outcomes	+ Help participant to translate into real-life gains such as at school or work
5. Future directions	+ Computerised CRT

change this, could you use a different mug?' but then she'd go 'but I have my favourite mug' (laughs).So it made it a bit more, I don't know, comfortable."

Participant 2: "It's nice to be on the same level (with parents)."

Mother 5: "[…]We are both doing as opposed to normally it's just [Participants name], so you know you're in it together as opposed to one leading the other. Yes, that was a really big positive."

3.8.2. Quality time together outside of the eating disorder

All of the AN participants and mothers commented that using the manual together had been beneficial as it had allowed them to spend some quality time together not discussing eating disorder issues, but on something that did feel beneficial:

Participant 2: "I guess it does bring you together a bit, to do something light hearted".

Participant 4: "I don't know if it is specific to me, but my dad is kind of, he wants to help but, he tends to relate everything to food which isn't always the most helpful thing (laughs)[…] this gave me time with him outside of that, where he felt he was helping and it was really good for him to get involved without putting his foot in it or walking on egg shells around me."

Participant 1: "[…] you feel guilty for putting them through it all, […] I know they probably feel a bit impotent sometimes because they are far away and because I won't let anybody help because I'm a grown up. [This] makes it like I'm being quite nice letting them help […] I don't know, it must be frustrating to feel powerless when I won't engage with anyone so this allowed that and that was beneficial…"

Mother 1: "[…] there was a reason to talk and it was lovely, and the fact that we spent most of the time laughing was also good. […] when we were asked to comment on how it went, I think most of it was just good fun and that was fantastic."

3.8.3. Family members facilitating reflecting

A number of AN participants had commented that reflecting on thinking styles with the guidance of a therapist had been difficult. However, when discussing the involvement of family members, all of the AN participants suggested that mothers or fathers had been helpful in aiding with this part of the intervention:

Participant 1: "I wouldn't really have extensively [engaged in reflection without mother]. I probably would have come to some kind of dead end conclusion quite quickly. I [would have a] quick look at the reflections [and think] how can you apply this to everyday life? I [would think] well 'oh no I'm not doing that' you know? It was like 'you could change this or change your breakfast'. […] If no one had been helping me to engage, I would have just gone 'no it's just not possible I don't have to engage with this anymore'. But if someone badgers me [that was different]."

Participant 1: "I think had I done it totally on my own, […] without mum I probably wouldn't have totally engaged with doing the reflective bits."

A number of mothers also felt that their involvement had been helpful with the refection. Two mothers also felt that their involvement here had been advantageous over a therapist:

Mother 1: "Sometimes [when] you have to engage with the therapist you think 'oh god' and you don't really trust them, but if it's somebody that you have a good relationship with you would be more honest."

Mother 6: "That's where we were helping mostly, with the reflection piece."

3.8.4. Stepping stone for more emotional discussions

Five mothers commented that working together on the CRT exercises had acted as a gateway for more emotional discussions:

Mother 1: "The only thing that I would add [is] the fact that [because] it's all about cold cognitions, [this] made it accessible and fun, and it just led into other conversations that were perhaps a bit more sensitive […] I suppose as a parent you're kind of thinking 'well I think we ought to talk about things' and you don't know how to do it other than to start getting emotional, so the non-emotional nature of this [… was] very helpful for leading onto more difficult discussions."

3.8.5. Not responsive to parent 'pushing'

Two of the mothers commented that they had sometimes found it difficult to get their children to complete some tasks, particularly if it had required the child to come out of their comfort zone. They also commented that they believed their child would have pushed themselves more had they been in the presence of a therapist.

Mother 5: "One of the main problems I had was getting [participant name] down to do it […], there was always something she would rather do, and I tried to have specific time, but still it was really hard, so I think that's a typical teenager-mum thing and I think that's quite hard, where as if we had been in a therapy situation, she would have done it."

Mother 6: "[participant name] was much more […] wanting to stay within her comfort zone, and had she worked with someone

who might have challenged that aspect a bit better […] I think that's quite difficult for a teenager, but with a therapist that would be different."

Mother 6: *"I think there is something about […] the relationship between […] parents and teenager […], that when you come together to do tasks, it has this very different flavour, and I don't think that is unique to CHILD, but it's a different relationship, its more formal. So when husband and I would say […] let's try and reflect […], then that's quite irritating[…].[…]CHILD was more likely to do it on her own [and] that would be less irritating and certainly working with me or husband for 6 weeks on those tasks that wouldn't work. It worked with husband in week 1 or 2 because they both had a laugh about it and experienced it together, [but] I think there is something about that therapy support that just frames it differently. That doesn't mean that it doesn't work though."*

3.8.6. Helping with familial traits

Four AN participants commented that they had been motivated to do the intervention with a family member in order to help family members with their own cognitive inflexibility, detail biases or perfectionism:

Participant 2: *"I just thought because my dad's quite rigid and stuff, I thought […] it would be good for my dad."*

Participant 1: *"When we were doing the introductory session I was thinking 'oh yeah this is totally like my dad' and he could really benefit from doing something like this."*

3.9. Raising awareness/insight of neuropsychological profile

A number of participants commented that a benefit of the treatment had been helping them to become aware and gain insight into their cognitive style. They also commented that practicing the tasks had given them the confidence to try and make some small 'real life' changes:

Participant 1:"By doing the tasks I was, maybe more aware of the fact that I could change. I think I already knew and I do try and change things in my routine because I know if I made the whole of my life a routine it would be really difficult to get out of, so I often try and […] slightly change the order of things […]. But by doing this regularly it made me be a bit more open to the fact that you could change things, it's just that bit higher up in your awareness. […] even if it was the case of thinking 'oh I could be more flexible here' and thinking about it, but then thinking 'well, actually I'm not going to be more flexible because I've decided I'm not', […] at least I considered it."

Participant 1: *"There are […]things like changing your seat at dinner or [on] the bus […] I know which seat I like, but maybe if I had to not sit on that one, it wouldn't be the end of the world, and then recognizing what I am doing and giving myself a little pat on the back and go […] well done me, I've done something different."*

Mother 3: *"It gave us a reason to talk about this, whereas otherwise we wouldn't have done. Just even talking about it, makes you realize that […] there are choices and you can do it in different ways."*

3.10. Real life applications/positive outcomes

Three AN participants and three mothers commented that they had been able to take the principles of CRT and apply them to different areas of life and make some functional gains:

Participant 4: *"[…] because I was mid-revision, because I'm doing maths, you have to look at the bigger picture and draw diagrams and stuff, and I found it kind of helped with that as well, it helped me, it helped me see the bigger picture."*

Mother 2: *"I thought 'my gosh I recognise that, that can be relevant for us'. And we thought about it and it had quite a miraculous change in CHILD's ability to complete the exam papers in the given time period and complete each section within the required amount of time, and that's the first time she'd ever done that."*

3.11. Future directions

Whilst discussing potential improvements to the manual, four AN participants and three mothers mentioned that they would like to see the manual in a computerised format:

Participant 1: *"Definitely the advantage of [it being computerised] would be you could have like a little app on your phone for doing that practice on your own, and […] when you are sitting on the bus or something you could play a little game on your own to keep you going and then once every now and then you sit down with your family and then do it in the book."*

Participant 4: *"You could make an (CRT) app."*

Mother 3: *"I do wonder if it would be better online, you know everybody loves online stuff."*

Mother 4: *"Online would be good, then you could keep adding new exercises, you wouldn't exhaust it, and […] that would save on costs and things."*

4. Discussion

This pilot study aimed to assess the feasibility and acceptability of CRT when delivered in a self-help format in collaboration with carers. Overall positive feedback from a qualitative interview suggested high levels of satisfaction and acceptability for both the self-help format and working with parents, with all participants commenting that they would recommend the treatment to others.

A discussion of the pros and cons generated numerous positives about CRT in a self-help modality such as convenience, spontaneity, and those who had prior experience of CRT with a therapist, remarking that it was a comparable treatment. Limitations of the self-help format were also raised, such as some individuals finding it difficult to find time to complete CRT tasks at home, as well as reflect on the CRT tasks without a therapist.

There were also a number of benefits of collaborating with a family member. Although the AN participants had mentioned that reflecting without a therapist had been difficult, all participants felt that a major benefit of working together with a family member was that it had helped them to reflect. A number of individuals commented that reflecting had been the most challenging aspect of CRT, and speculated that without having a family member to help with this, they may have avoided it all together.

There was also evidence to suggest that treatment in this format may be beneficial for family stress and relationships. A majority of patients and parents commented that this treatment had been beneficial as its playful and fun nature had allowed them to spend time together outside of the eating disorder. One family commented that the CRT tasks had even acted as a 'gateway' for more emotional and difficult conversations, which may not have taken place otherwise. This finding is an important one, as AN is associated with significantly high carer stress and burden

(Treasure, 2001; Graap et al., 2008), and therefore treatments that involve family members and carers are valuable (Treasure et al., 2003).

Some AN participants felt that the collaboration had also been beneficial in terms of helping with their carers own neuropsychological task performance. This is another important finding as current research shows that the cognitive profile observed in AN can also manifest in unaffected family members, suggesting that these traits may be familial (Holliday et al., 2005; Roberts et al., 2010).

A further benefit acknowledged by the participants in this study was that CRT had allowed them to develop awareness and insight into their cognitive style. Although sometimes difficult, this increased awareness had opened up the possibility of generalising the skills from the task to real-life and make functional gains.

An important challenge noted by parents in this study was the difficulty in getting their offspring to sometimes do the tasks, particularly when these required the child to move outside of their comfort zone. This is not particularly surprising given that parents are not trained as therapists. It is noteworthy that the parents who found this a challenging element of the treatment were parents with adolescent children. This could suggest whilst CRT may be an appropriate intervention for children and adolescents, when it is facilitated by parents alone it could be particularly challenging and may not be appropriate for all families.

At the same time, the results of this study clearly show that creating a shared space "free" from eating disorder talk was helpful for both AN participants and parents.

It is also important to note the mean time spent on the CRT tasks per week as reported by the patients ranging from 12.07 to 20 minutes over the 6 weeks. These data suggest that there may be a discrepancy between what would routinely be administered in clinic to what patients may carry out themselves. This should be taken into account in future research, perhaps with future studies giving more specific guidance on dosage to allow for comparisons with clinician-led CRT.

Overall, these preliminary findings add to the growing literature supporting CRT for AN. To date CRT in both individual and group formats have received positive feedback from patients and therapists with noted improvements to motivation, cognition and quality of life (Brockmeyer et al., 2014; Dingemans et al., 2014; Lock et al., 2013). Interestingly, qualitative feedback from both clinician-led and self-help approaches have elicited the same strengths and challenges. The light-hearted and playful nature of CRT was also reported as a positive in previous qualitative studies (Whitney et al., 2008; Easter and Tchanturia, 2011).

In addition to the positive qualitative feedback gathered in this study, individual improvements on neurocognitive performance in both patient and parent groups were also noted. Although this is encouraging, practise effects of these tasks on performance cannot be ruled out.

This study had no directional hypothesis, but following the focus groups there was the distinct impression that with future developments, treatment of this sort might be a useful step for families in the journey towards recovery.

This study carries important clinical implications. Firstly, this study suggests that self-help is an acceptable modality for CRT delivery. This increases the accessibility of this treatment to patients and families who may not otherwise have access to it. Second, as this treatment, for the most part appeared to be beneficial to care-giver stress and burden (with the exception of some of the challenges that may present with younger patients) (Graap et al., 2008), the positive impact of involving family members in treatment is well accepted across different psychiatric conditions (Waters and Barrett, 2000; McLean et al., 2003; Prestwich et al., 2014).

Although the findings from this study are encouraging, a limitation of this study is its small sample size and so the findings are of a preliminary nature. Further studies utilising larger samples sizes are needed. For this reason the neuropsychological outcomes should also be interpreted with caution. A further limitation is the fact that both the WCST and the ROCFT are known to have practice effects, that could have contributed to the improvement in time two scores. Future work could examine how this format of CRT impacts on patient motivation for further psychological work, and could also consider developing a computerised version of the self-help CRT manual as suggested by a number of participants in the present study.

In conclusion, this study demonstrates that self-help CRT in collaboration with family members is a feasible and acceptable form of treatment with numerous benefits for both patients and carers.

Contributors

KL—Study design, recruitment for study, conducted training sessions and focus groups, analysis data, writing manuscript.

JT—Recruitment for study, writing manuscript.

KT—Study design, recruitment for study, conducted training sessions and focus groups, writing manuscript.

Conflict of interest

The authors have no conflict of interest to declare.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.psychres.2014.12.008.

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CHAPTER 6

STUDY 4: EXPLORING EMOTION RECOGNITION IN ADULTS AND ADOLESCENTS WITH ANOREXIA NERVOSA USING A BODY MOTION PARADIGM

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RESEARCH ARTICLE

Exploring Emotion Recognition in Adults and Adolescents with Anorexia Nervosa Using a Body Motion Paradigm

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Abstract

Objective: There is consistent evidence of difficulties in social cognition in adults with anorexia nervosa (AN), but less is known about adolescents. The aim of this study was to investigate the ability to recognise emotion expressed in body movement in adults and adolescents with AN.
Method: One hundred and ninety-three females participated in the study (AN = 97: 61 adults and 36 adolescents). The performance of participants with AN on a body emotion recognition task was compared to age-matched healthy controls (HC = 96).
Results: AN participants were significantly worse than HC recognising sadness, with adolescent AN participants showing worse performance overall. There were no difficulties in the recognition of other emotions.
Discussion: The results partially support previous studies and the literature on facial emotion recognition, showing poorer recognition of sadness in AN. The results also suggest that difficulties in emotion recognition through body movements may be more subtle than other socio-emotional difficulties observed in AN.

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Keywords
Emotion recognition; anorexia nervosa; eating disorders; point light; body motion

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Adults with eating disorders (EDs), and particularly with anorexia nervosa (AN), demonstrate difficulties in social cognition (Caglar-Nazali et al., 2014; Oldershaw, Hambrook, et al., 2011), exhibiting problems in emotional intelligence (Hambrook, Brown, & Tchanturia, 2012), high levels of social anhedonia (Tchanturia et al., 2012), reduced emotion expression (Claes et al., 2012; Davies, Schmidt, Stahl, & Tchanturia, 2011), and poor social functioning (Harrison, Mountford, & Tchanturia, 2014; Tchanturia, Hambrook, et al., 2013) compared to healthy controls (HC). Several theories have proposed that socio-emotional difficulties contribute to the development and/or maintenance of the ED (Arcelus, Haslam, Farrow, & Meyer, 2013; Fox & Power, 2009; Treasure & Schmidt, 2013; Wildes, Ringham, & Marcus, 2010), but further understanding of the mechanisms involved in these difficulties is needed in order to design effective interventions.

An important aspect of social and emotional processing is the visual perception of emotions, including the exchange of information through facial expression, eye gaze, and body movement (Frith & Frith, 2007). Some of the mechanisms underlying the difficulties exhibited by people with AN may be related to the way in which individuals with AN interpret visually mediated social messages, intentions, and emotions. For example, research has shown attentional biases in individuals with AN towards angry, sad and rejecting faces (Aspen, Darcy, & Lock, 2013; Cardi, Di Matteo, Corfield, & Treasure, 2013; Cserjesi, Vermeulen, Lenard, & Luminet, 2011; Harrison, Sullivan, Tchanturia, & Treasure, 2010), hypervigilance to threat-related cues (McFillin et al., 2012), and avoidance of accepting faces (Cardi et al., 2013).

A majority of studies examining the ability to infer emotional states in others (i.e. emotional Theory of Mind) using the Reading the Mind in the Eyes task (Baron-Cohen, Wheelwright, Hill, Raste, & Plumb, 2001) in individuals with EDs (13 in total) have demonstrated that participants with AN are less accurate at identifying emotional states in people's eyes, compared to HC (Tchanturia, Dapelo, Harrison, & Hambrook, 2015). However, findings from studies examining emotion recognition from faces have been more inconsistent (Tchanturia et al., 2015).

Currently, there is a distinct lack of research investigating socio-emotional processing in adolescents with AN. As adolescence is a critical time for social–cognitive development (Blakemore, 2012), social emotional ability at this time period is of particular relevance in understanding the consequences of this disorder. Although limited, the available literature suggests that adolescents with AN may display similar socio-emotional difficulties as adults with AN. A series of studies by Zonnevijlle-Bender, van Goozen, Cohen-Kettenis, van Elburg, and van Engeland (2002) and Zonnevylle-Bender et al. (2004) suggested that adolescents with AN showed higher levels of alexithymia, as well as performing significantly worse on experimental measures of facial emotion recognition, compared to matched HCs (Zonnevijlle-Bender et al., 2002), along with a comparable poor performance to adult AN participants (Zonnevylle-Bender et al., 2004). Lule et al. (2014) also found a decreased ability to recognise disgust in adolescents with AN. There is also preliminary evidence of reduced facial emotion expression in adolescents with AN (Rhind, Mandy, Treasure, & Tchanturia, 2014). Albeit limited, the available data suggests that further investigation of social cognition in adolescents with AN is warranted.

Facial emotion recognition and expression are only part of nonverbal communication, another important aspect being body language (App, McIntosh, Reed, & Hertenstein, 2011). In fact, it has been proposed that body language can communicate both the emotion and the action tendency associated with the emotion (e.g. fear, therefore escape) (de Gelder, 2006; Demeijer, 1989), and there is evidence that the same brain regions that are known to be involved in the perception of facial emotion expression and behaviour are also involved in the processing of emotional body language (de Gelder, 2006). It has been demonstrated that specific emotional states can be inferred by observing particular body movements (Atkinson, Dittrich, Gemmell, & Young, 2004; Demeijer, 1989; Heberlein, Adolphs, Tranel, & Damasio, 2004), and there is evidence that certain patterns of body movements may be specific to certain emotions (Wallbott, 1998). However, in contrast to the large amount of studies looking at facial emotion recognition, emotion recognition from body motion has received little attention in ED.

Point-light walker (PLW) procedures (Heberlein et al., 2004) have been used to assess recognition of emotion expressed through body movements in different clinical populations. For example, problems with emotion recognition have been consistently demonstrated in the schizophrenia literature when using PLW (Brittain, Ffytche, & Surguladze, 2012; Couture et al., 2010), and similar results have been described for individuals with autistic spectrum disorders (Hubert et al., 2007; Nackaerts et al., 2012). Given the evidence of the high prevalence of autistic traits in people with AN (Baron-Cohen et al., 2013; Gillberg, 1983; Tchanturia, Smith, et al., 2013; Treasure, 2013; Zucker et al., 2007), some difficulties in this ability are to be expected.

To our knowledge, only one study has explored the ability to recognise emotions from body motion in individuals with AN using PLW. Zucker et al. (2013) found that, compared with HC and weight restored participants, individuals with current AN were less accurate at identifying sadness, and more consistent than HC in recognising anger. In this study, weight restored participants showed similar performance to that of the HC (Zucker et al., 2013).

The current study aims to further build on these findings by first, investigating emotion recognition through body motion in a large sample of participants with AN using the PLW procedure. Second, we aim to investigate developmental differences in emotion recognition abilities in AN by comparing the performance of adults and adolescents.

Materials and methods

Participants

Participants were 193 females: 97 (61 adults; 36 adolescents) with AN and 96 HC (69 adults; 27 adolescents), ranging in age from 11 to 55 years. The AN participants were recruited from Specialist Eating Disorder clinics and the local community. AN participants received a DSM-5 diagnosis of AN by using the Eating Disorder module of the Structured Clinical Interview for DSM-IV-TR Axis I Disorders (SCID-I) (First, Gibbon, Spitzer, & Williams, 2002). Measures of height and weight were also routinely collected. The inclusion criteria for AN participants older than 18 years of age was a BMI of less than 18.5. For AN participants younger than 18 years of age percentage ideal body weight (%IBW) calculations were made. Ideal body weight measurements indicate the percentage of the individual ideal body weight for their height and age. Participants with a %IBW of less than 90 were included in this study.

HC participants were recruited from the university and local community. Absence of ED symptoms in HC was evaluated using the ED module of the SCID and the Eating Disorder Examination Questionnaire (EDE-Q), along with measures of height and weight. The same BMI threshold was applied, this time, BMI being higher than 18.5 for those over 18 years old (adults) and the %IBW over 90 for those of under 18 years (adolescents). HC and AN sample did not differ significantly in age.

Measures

Structured clinical interview for DSM-IV-TR Axis I Disorders; SCID-I: (First et al., 2002)

The SCID is a semi-structured clinical interview aimed to assess axis I disorders according to the DSM-IV (American Psychiatric Association, 2000). In this study, the ED module (i.e. module H) was used to assess the presence and history of ED. In order to update the interview to DSM-5 criteria, criterion D (i.e. amenorrhea) was not required for AN diagnosis, and the frequency for binges and purges was reduced to once a week to assess the presence of bulimia nervosa in HC.

Body mass index (BMI—kg/m^2) for adult and % ideal body weight (%IBW) for adolescents

BMI and %IBW were calculated based on measurements taken during the testing session.

Eating Disorder Examination Questionnaire; EDE-Q: (Fairburn & Beglin, 1994)

The EDE-Q is a 36-item self-report measure that assesses cognitions and behavioural features of ED. In the current study, internal consistency for EDE-Q scales ranged from $\alpha = 0.77$ to $\alpha = 0.97$.

Hospital Anxiety and Depression Scale; HADS: (Zigmond & Snaith, 1983)

The HADS is a 14-item self-report questionnaire developed to assess anxiety and depression among patients of non-psychiatric clinics and shown to have good validity and reliability (Bjelland, Dahl, Haug, & Neckelmann, 2002). Internal consistency for the anxiety scale was $\alpha = 0.88$, and for the depression scale was $\alpha = 0.83$.

Autism Quotient; AQ-10: (Allison, Auyeung, & Baron-Cohen, 2012)

The AQ-10 is a shorter version of the original Autism Quotient (Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001) and has been used in ED (Tchanturia, Smith, et al., 2013). A cut-off of 6 has been established to indicate clinical severity of autistic features. In this study, internal consistency was $\alpha = 0.64$.

Emotion recognition from body movement. Point-light walkers task (PLW)

Originally created by Johansson (1973) to investigate human motion. It was then adapted to explore human ability to infer emotional states expressed through bodily motion (Heberlein et al., 2004). The present study employed the same methodology developed in previous studies with video clips of 40 point-light walkers (Atkinson, Heberlein, & Adolphs, 2007). For the development of this task, actors were filmed walking from left to right, whilst portraying one of four emotions (anger, fear, happiness, or sadness) or an emotionally neutral state. The actors were filmed in the dark and had small lights attached to their wrists, ankles, knees, elbows, outer hips, waist, outer shoulders, and head. Thus, the stimuli appeared as white dots on a dark background (Atkinson et al., 2004).

There were 40 trials (4 emotions × 8 clips + 8 neutral clips) and five different randomised running orders were used. Participants rated which emotion was being portrayed from the five alternative forced-choice words (angry, afraid, happy, sad, or neutral) presented on a card. Five practice clips were used to explain the task.

A proportional correct scoring method, previously used with stimuli of this type, was employed to score participant's answers (Heberlein et al., 2004). In a pilot study, 15 'reference' HC participants rated the emotional clips in the way described above, with the exception that there were no 'neutral' clips and no 'neutral' answer choice (i.e. 32 clips). Percentages were calculated for the amount of times each stimulus was labelled as a particular emotion by the reference group. These percentages then formed the basis of the partial correctness scoring for the main study. For example, if a clip was labelled as 'happy' by 70% of the reference group, 'angry' by 20% of the reference group, and 'sad' by 10% of the reference group, then if a participant in the main study labelled the same clip as 'happy' they would achieve the highest score of 1.0 (0.7/0.7), if they labelled it as 'angry' they would score 0.28 (0.2/0.7), and if they labelled it as 'sad' they would score 0.14 (0.1/0.7). All other answers would receive a score of 0. In the main study, the total score for each emotion corresponds to the sum of the scores obtained by the participant on each of the eight clips that represent the emotion (i.e. the maximum score is 8 for each emotion category). This scoring method accepts that a certain degree of variability in the interpretation of emotions from body movements is common, for example a body movement can be perceived as both sad and fearful (Heberlein et al., 2004).

Procedure

Participants attended one session for the study. After completion of BMI measures and the PLW task they filled self-report questionnaires. The study was approved by the NHS Research Ethics Committee, reference number 13/LO/0201 and 12/LO/2015. Informed consent was obtained from all participants.

Statistical analysis

Data were analysed using the statistical software STATA 12.0 © (StataCorp LP). Visual inspection of histograms revealed that the data for each of the emotion variables was negatively skewed. Standard transformations were not able to normalize the data, and further inspection revealed that the distributions differed between the AN group and the HC group in terms of shape and scale (variability), meaning that the data did not fulfil the assumptions of nonparametric tests (e.g. Mann Whitney *U* test). We therefore analysed the data using median regression (more generally known as quantile regression (Cade & Noon, 2003; Koenker, 2005)), which is a more robust alternative to linear regression and suitable for modelling skewed data. Standard linear regression estimates the relationship between mean of a response distribution and a set of independent or predictor variables; whereas the median regression models the relationship between median of a response distribution and a set of predictor variables. Group comparison can be made in a median regression by including a binary group indicator (in this study, 0 = HC, 1 = AN) as independent variable in the regression model. The regression coefficient for group represents the differences in medians between groups

For each emotion variable, a median regression was performed to estimate and test for differences in the medians between the AN and HC groups. The effects of group (i.e. the median differences) were adjusted for the effect of age, %IBW, BMI, anxiety, depression, and autistic traits by including them as covariates in the median regression models. Each of the potential confounding variables was tested individually in a separate median regression model. The variables that were found to be individually associated with the outcome variable at a *p*-value level less than 0.05 were included in the adjusted model described above.

Differences between the total AN group and HC group were explored first, with a subsidiary analysis investigating the AN sample split into adults and adolescents.

Results

Table 1 shows the demographic information of the total AN and HC groups. As expected, there was a significant difference between the groups with regard to BMI and clinical characteristics, such as eating disorders symptoms, anxiety, depression, and autistic traits.

Group comparisons for each emotion

Figure 1 shows the median for each emotion for both the AN and the HC groups. Median regressions are shown in Table 2.

Table 1 Participant demographics and clinical measures

	AN				HC				Cohen's *d*
	N	Min	Max	Mean (SD)	*N*	Min	Max	Mean (SD)	
Age	97	11.00	47.00	22.40 (8.32)	96	11.00	53.00	23.72 (9.80)	0.15
BMI * (adults only)	61	11.60	18.40	15.44 (1.68)	69	18.74	28.40	22.34 (2.42)	3.30
W4H * (adolescents only)	36	61.07	89.65	80.65 (6.69)	27	90.18	128.82	100.62 (9.95)	2.46
EDE-Q Rest *	97	0.00	6.00	3.56 (1.80)	96	0.00	4.40	0.81 (0.94)	1.92
EDE-Q Eat C *	97	0.00	6.00	3.40 (1.46)	96	0.00	2.40	0.31 (0.47)	2.86
EDE-Q Sh C *	97	0.13	6.00	4.45 (1.56)	96	0.00	5.13	1.33 (1.06)	2.35
EDE-Q Wt C *	97	0.20	6.00	3.74 (1.62)	96	0.00	4.20	0.96 (0.94)	2.11
EDE-Q Global *	97	0.19	6.00	3.79 (1.44)	96	0.00	3.83	0.85 (0.76)	2.56
Age of Onset	97	8.00	37.00	16.40 (5.51)					
Length of Illness (years)	97	0.00	37.00	6.20 (7.22)					
HADS-A *	97	0.00	21.00	11.20 (5.08)	96	0.00	9.00	4.05 (2.60)	1.78
HADS-D *	97	0.00	21.00	11.67 (4.90)	96	0.00	9.00	3.63 (2.04)	2.15
AQ-10 *	97	0.00	9.00	3.92 (2.13)	96	0.00	5.00	1.87 (1.34)	1.16

BMI = body mass index; W4H = percentage weight for height, EDE-Q Rest = Eating Disorder Examination Questionnaire Restraint; EDE-Q Eat C = Eating Disorder Examination Questionnaire Eating Concerns; EDE-Q Sh C = Eating Disorder Examination Questionnaire Shape concerns; EDE-Q Wt C = Eating Disorder Examination Questionnaire Weight Concerns; EDE-Q Global = Eating Disorder Examination Questionnaire Global Score; HADS-A = Hospital Anxiety and Depression Scale Anxiety subscale; HADS-D = Hospital Anxiety and Depression Scale Depression subscale; AQ-10 = Autism Quotient 10.
(*) Mean difference is statistically significant ($p < 0.01$).

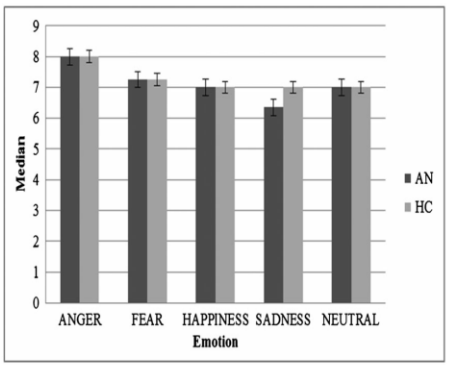

Figure 1 Medians and standard errors for each emotion for AN and HC groups

Table 2 Median regression for each emotion

Emotion	Regression coef. for group (AN vs. HC)	SE (coef.)	*p*-Value	95% CI
Neutral	0.00	0.21	1.00	(−0.42, 0.42)
Fear	0.00	0.14	1.00	(−0.27, 0.27)
Happiness	0.00	0.20	1.00	(−0.40, 0.40)
Sadness*	−0.64	0.25	0.01	(−1.14, −0.14)

Regression coef. = coefficients represent the estimated differences in medians between AN and HC groups; AN = anorexia nervosa; HC = healthy controls; SE = standard error; CI = confidence interval.
(*) Regression is statistically significant ($p < 0.05$).

Neutral

There were no significant differences between AN and HC groups on neutral clips (difference in medians = 0.00, $p = 1.00$).

Anger

Because of lack of between group data variability, it was not possible to compute median regression for the anger clips. Visual inspection of the medians for the AN group and HC group suggested that there were no differences between groups (AN median = 8.00, HC median = 8.00). Further inspection of the shape of the distribution of this variable indicated that it was similar for both groups (AN and HC); therefore, Mann Whitney *U* test was carried out. The test confirmed that there were no significant differences between AN and HC ($U(191) = 5{,}071.00$, $p = 0.23$).

Fear

There were no differences between the AN and HC groups in recognising fear (difference in medians = 0.00, $p = 1.00$).

Happiness

There were no significant differences recognising happiness between AN and HC groups (difference in medians = 0.00, $p = 1.00$).

Sadness

There was a significant difference between the medians of AN and HC groups, with the AN group being less accurate at recognising sadness (difference in median = −0.64, $p = 0.012$). Group, age, and %IBW were significant independent predictors of the outcome. However, when added together to the median regression model, %IBW lost significance. Group and age remained significant predictors, with younger participants exhibiting worse

performance (difference in median = −0.58, $p = 0.028$). Together they predicted 4.19% of the variance.

The AN participants who did not correctly recognise and label the sadness stimulus, most commonly misinterpreted the clips as neutral (mean percentage of participants for the 8 sad clips = 17.5%), followed by anger (mean percentage of participants = 6.7%), happiness (mean percentage of participants = 2.7%), and then fear (mean percentage of participants = 2.1%). Further inspection of the data indicated that the results were not because of the systematic misinterpretation of one specific clip, but all the sad clips had been misinterpreted by at least some AN participants.

Adult versus adolescent analysis

A further analysis of the sadness emotion, which had shown difficulties in the total AN group with age as significant factor, was carried out by splitting the sample into adults (≥18 years old) and adolescents (<18 years old). Table 3 describes means and medians for each group. This new variable was included as a covariate in the median regression along with the interaction effect of the clinical group (i.e. AN or HC) and the age group (i.e. adult or adolescent). The interaction was statistically significant (difference in median = 0.089, $p = 0.001$) meaning that AN versus HC group difference varied between the adult and adolescent group. Adolescents with AN exhibited worse performance than the rest of the participants.

Discussion

The aim of the study was to explore emotion recognition through body movements using a group of adolescents and adults with AN. The findings demonstrated that overall, there was poorer performance in recognising sadness in the AN group compared to HC. There was no evidence of difficulties in the recognition of fear, anger, and happiness in body motion stimuli.

Our results are in agreement with previous findings from Zucker et al. (2013) who reported difficulties in the recognition of sadness in AN participants using point-light walkers (PLW). In addition, our findings are consistent with the previous literature evaluating facial emotion recognition in AN. For example, Kucharska-Pietura, Nikolaou, Masiak, and Treasure (2004) reported poorer recognition of sadness in faces in AN, and the same results have been found by Pollatos, Herbert, Schandry, and Gramann (2008), and Castro, Davies, Hale, Surguladze, and Tchanturia (2010). Taken together, these findings may be suggestive of specific difficulties in the recognition of sadness in AN.

Table 3 Mean and medians for sadness recognition for AN adults, AN adolescents, HC adults, and HC adolescents

	N	Mean	S.D.	Median
AN adolescents	36	5.45	1.45	5.68
AN adults	61	6.45	1.53	7.00
HC adolescents	27	6.47	1.40	7.00
HC adults	69	6.48	1.42	7.00

N = number of participants in the group; SD = standard deviation; AN = anorexia nervosa; HC = healthy control.

Moreover, a study using electroencephalography along with an emotion recognition task found that the difficulties recognising sadness in AN were associated with an increase in N200 amplitudes, which the authors related to an increase in attentional demands for the classification of sad faces (Pollatos et al., 2008). This would be consistent with studies on attentional bias that report a bias towards sad faces (Cserjesi et al., 2011). It might be that individuals with AN have difficulties processing signs of sadness in faces and body, requiring more attentional resources to interpret these cues, and therefore exhibiting longer reaction times in attentional bias tasks. In this study, response times were not measured, and therefore we are unable to test this hypothesis. However, future studies might provide more insight on the mechanisms explaining the difficulties on sadness recognition in people with AN.

In our study there was a significant interaction between group (AN or HC) and age, whereby younger participants with AN appeared to show poorer recognition of sadness. Further exploration of this interaction indicated that adolescents with AN showed more difficulties in sadness recognition compared to adults. This is the first study to explore emotion recognition through body movement in adolescents with AN, and our findings are consistent with studies on facial emotion recognition that have shown difficulties in adolescents with AN (Zonnevijlle-Bender et al., 2002; Zonnevylle-Bender et al., 2004). Our results are also consistent with studies on facial emotion recognition in non-clinical populations that have demonstrated a continuum in the process of learning to recognise emotion expression throughout development (Herba & Phillips, 2004). Poorer performance in adolescents with AN could be because of the effects of starvation at a critical period of brain maturation disturbing the normal developmental trajectory of emotion recognition skills. Further studies with children and adolescents with AN utilising fMRI to delineate the neural underpinnings of emotion recognition are needed to confirm this.

Our study findings indicate that AN participants who were poorer at recognising sad clips, often misinterpreted them as neutral. It can be speculated that having difficulties in correctly recognising sadness in others can have negative consequences for social interaction, as it makes it hard to recognise the needs of others and respond appropriately, for example, by showing empathy. The evidence from studies on decision making suggest that sadness elicits compassion and leads to cooperation among people (Polman & Kim, 2013). Thus, having difficulties recognising sadness could have a negative impact on social cooperation. Furthermore, the finding that adolescents with AN were the poorest at recognising sadness highlights the need to support adolescents with AN in their social development, especially because adolescence is a time of rapid social development, where social relationships are particularly salient.

Our findings suggest that difficulties in emotion recognition in AN differ from those described for people with schizophrenia (Brittain et al., 2012; Couture et al., 2010) and autism (Hubert et al., 2007; Nackaerts et al., 2012; Philip et al., 2010). Unlike these clinical groups, individuals with AN do not seem to exhibit a generalised problem with emotion recognition from body motion.

Moreover, in our study, autistic features, as measured by the AQ-10, were not associated with emotion recognition performance in PWL task. One possible explanation for this lack of association could be that although individuals with AN and ASD have similarities in cognitive profiles, there may be distinct differences in the emotional difficulties shown by each group (Oldershaw, Treasure, Hambrook, Tchanturia, & Schmidt, 2011); therefore, although some individuals with AN show elevated levels of autistic traits, they may not meet the clinically defined cut-off for a diagnosis of autism, and this may not translate into the same emotion recognition difficulties that are observed in individuals with a diagnosis of ASD. In addition, the majority of the ASD literature is based on male participants, whereas experimental studies of emotions in ED field are conducted on female participants including the current study. Finally, it is worth noting that in this study, the AQ-10 did not have a satisfactory internal consistency; therefore, results on autism should be interpreted with caution.

The relative subtlety of our findings in comparison to stronger evidence of difficulties in other areas of emotion recognition for those with AN (Caglar-Nazali et al., 2014; Oldershaw, Hambrook, et al., 2011) could suggest that emotion recognition through body movement may be considered a comparative strength in AN. It has been suggested that because body language provides information about both emotional states and their associated intentions, it may be a less ambiguous signal compared to facial emotion expression, and therefore easier to recognise, label, and respond to (de Gelder, 2006).

It should be noted that the study might be limited by the negative skewing of the emotional recognition data for both AN and HC participants, with a proportion of the participants achieving maximum scores. This may suggest a ceiling effect in the case of anger and could explain why an enhanced ability to identify anger in AN was not found in this study. Moreover, even though we used the exact same methodology utilized in previous studies (e.g. Heberlein et al., 2004), the absence of neutral clips and answer choices in the pilot study, which provided the information for the proportional correct scoring method, might have had an impact on the study results. Additionally, as a majority of AN cases are female, the present study only included female participants. However, given the known gender differences in the recognition of emotions in facial expressions (Hall & Matsumoto, 2004; Thayer & Johnsen, 2000) differences in body emotion recognition between men and women may also be expected, and future studies could be conducted to address this issue.

In summary, this study explored emotion recognition in body motion in a large group of participants with AN, and it is the first to investigate this in adolescents with AN. Its results are important for the field as they replicate previous findings of difficulties in sadness recognition in AN. As the AN group's difficulties were confined to sadness, the results also suggest that difficulties in emotion recognition through body movements may be fairly subtle in comparison to other socio-emotional difficulties observed in this population. This information could be used in the development of future treatments targeting emotional skills. In addition, the greater impairment exhibited by adolescents with AN in this study highlights the importance for future research to continue to focus on the adolescent AN population.3

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CHAPTER 7

STUDY 5: EMOTION EXPRESSION AND ASSOCIATED CLINICAL FACTORS IN CHILDREN, ADOLESCENTS AND ADULTS WITH ANOREXIA NERVOSA

7.1 Introduction

Anorexia Nervosa is associated with social and emotional difficulties (Bruch, 1962), which are considered to pre-date the onset of the disorder. For example, problems in making and sustaining friendships and higher levels of bullying during childhood (Davies, 2004; Doris et al., 2014; Schutz & Paxton, 2007; Treasure & Schmidt, 2013). Such difficulties are thought to be one of the maintaining factors of the disorder (Ohmann et al., 2013; Treasure & Schmidt, 2013). Individuals with AN experience emotions and social interactions as highly problematic, as well as being more likely to report a poor social network and lack of social support than healthy controls (Hartmann et al., 2010; Tchanturia et al., 2013a; Tiller et al., 1997). In addition, numerous difficulties in socio-emotional processing in individuals with AN have been observed experimentally, such as emotion recognition (Oldershaw et al., 2011), theory of mind (Tchanturia et al., 2004b), alexithymia (Nowakowski et al., 2013) and social anhedonia (Harrison, Mountford, & Tchanturia, 2014; Tchanturia et al., 2012a). There is also evidence of their persistence following recovery, as well as emerging evidence of similar difficulties in children and adolescents with AN (Davies et al., 2013; Lang et al., 2015a; Zonnevijlle-Bendek et al., 2002) (Davies et al., 2013; Lang et al., 2015; Zonnevijlle-Bendek et al., 2002).

Individuals with AN also appear to have difficulties with emotion expression (Caglar-Nazali et al., 2014; Cardi et al., 2014; Claes et al., 2012; Davies et al., 2011). Facial expressions are known to be universal and are critical in signaling intentions to others and eliciting social responses in interactions (Izard & Izard, 1977). Two studies have described altered emotion expression in individuals with AN with stimuli designed to elicit a specific emotional response. Davies et al. (2011) found that adults with AN displayed less positive emotion than healthy controls (HC) whilst observing a positive film clip, despite subjectively reporting feeling the same levels of positive emotion as HC. The study also reported that patients with AN looked away significantly more during the negative clip. These findings were recently replicated in children and adolescents with AN (Rhind et al., 2014).

The social difficulties observed in AN have been shown to correspond with the high morbidity rates observed in AN and negatively impact treatment outcome (Zucker et

al., 2007). In particular, difficulties in signaling your own emotional state are likely to lead to poor treatment engagement and prognosis, as many psychological therapies rely on communicating one's own emotional state and intentions. In addition, suppression of emotional expression is associated with problematic relationships and limited friendship groups, which may hinder the use of social support and often contributes to maintenance of the illness (Doris et al., 2014; Treasure & Schmidt, 2013).

It is therefore important to investigate differences in emotion expression further and in particular the associated mechanisms and characteristics, for example illness severity and co-morbidities. A recent study by Lang et al. (2015b) found that compared to patients of an older age group, younger individuals with AN displayed the greater difficulties in recognizing emotions through body movements, suggesting that emotion processing may be more difficult for younger age groups with AN. Adolescence is a time of pubertal change, with significant amounts of hormone change and rapid brain development taking place (Blakemore & Choudhury, 2006). It is also a crucial time of social cognitive development, whereby many novel and complex social situations are experienced, aiding the development of social behaviours and abilities such as metalising. Differential social experiences during this time can idiosyncratically affect developmental brain processes, such as pruning (Blakemore, 2012b). It is therefore important to consider the consequences of starvation on hormonal changes and brain development, as well as social withdrawal and isolation due to ED pathology, during this time on social cognitive development for young people with AN, and investigate the effect of age on emotion expression in more depth.

Examining the underlying mechanisms associated with poor emotion expression could be used to develop more targeted treatments for AN. Historically, treatment of eating disorders (ED) has focused on changing illness related symptoms. However, research findings and clinical observations regarding socio-emotional difficulties are being translated into clinical practice, and treatments are being tailored accordingly broadening treatment goals (Fairburn et al., 2013; Lynch et al., 2013; Schmidt et al., 2012; Tchanturia et al., 2014b). For example one treatment module targeting socio-emotional difficulties in anorexia is cognitive remediation and emotion skills training (Money et al., 2011)(CREST)), which places a greater emphasis on

management and expression of emotions, as well as positive emotion recognition skills (Tchanturia, 2011; Tchanturia, Dapelo, Harrison, & Hambrook, 2015). CREST and its predecessor, cognitive remediation therapy (CRT) are both based on the maintenance model of AN (Treasure & Schmidt, 2013), aiming to increase the patient's quality of life by decreasing cognitive rigidity and increasing awareness of emotions and social communication skills (Davies et al., 2012; Money et al., 2011).

With this in mind the current study aimed to build on the current literature by: 1) Investigating emotion expression in an age diverse group of individuals with AN; 2) Investigate demographic and clinical correlates of emotion expression within the AN group.

7.2 Method

7.2.1 Participants

Sixty-six participants with a DSM-5 diagnosis of AN were recruited for the study (age range 11-47). Child and adolescent AN participants (N=36) were recruited from the Child and Adolescent Eating Disorder Service at the South London and Maudsley (SLaM) NHS Trust. Adult AN patients were recruited from both the SLaM inpatient and outpatient treatment programmes, the Vincent Square eating disorder clinic, and also from advertisements on the eating disorder charity BEAT's website. Participants were included in the study if they had a body mass index (BMI) of 17.5 or under (for adults, >18 years), or an ideal body weight (IBW) of 90% or under (for children and adolescents, < 18 years). Exclusion criteria included a diagnosis of learning disability, psychosis or Autism Spectrum Disorder (ASD).

Seventy-five age and ethnicity matched controls took part in the study. The ages of the HC group ranged from 11-53 years. N=39 of the HC participants were children and adolescents. All HC participants had a BMI over 17.5 (for adults) or an IBW of 91% or over (if <18 years of age). HC participants were recruited through advertisements in the local community. Exclusion criteria for the HC group included current or history of a mental health problem, or similar in first degree relatives.

7.2.2 Measures

7.2.2.1 Experimental stimuli

The current study used the same experimental methodology described in Davies et al., (2011). Participants were presented with positive ('Four Weddings and a Funeral'), negative ('Shadowlands') and neutral (simulated waves) film clips. The duration of the emotive clips were approximately three minutes long each.

Coding for emotion expression

Emotion expression during the positive and negative film clips was coded using the Facial Expression Coding System (FACES, (Kring & Sloan, 2007)). Facial expression during the neutral film clip was not coded. The purpose of this clip was to obtain a baseline for facial affect and to eliminate possible carry-over effects produced by the two emotion-inducing film clips. FACES is a global rating system, defining an expression as any change in the face from neutral, to non-neutral and then back to neutral. Expressions are only defined as 'positive' or 'negative', and not assigned a more definitive label (e.g. happiness). Each expression is coded for valence (positive or negative), intensity (1-4) and durations (seconds). A frequency count for each time the participant looks away during the clip is also coded.

Two authors (EL, EM) coded the clips, and a first author (KL) rated 15% of the sample. The Kappa for the two researchers was .70 (substantial agreement) for the positive film clip and .90 (perfect agreement) for the negative film clip.

7.2.2.2 Self-report measures

Positive and negative affect scale (PANAS (Watson et al., 1988)): A 22-item scale, containing items measuring both positive and negative affect. Participants indicate how they currently feel using a 4-point Likert scale for each adjective. The PANAS was completed immediately after viewing each clip. Participants were also asked if they felt any other emotion not listed and if they had seen the film clip before. Cronbach alpha for this sample was .70

Eating Disorder Examination Questionnaire (EDE-Q (Fairburn & Beglin, 1994)): A 36-item scale assessing eating disorder psychopathology. Clinical criteria cut-off adopted was a global score of higher than 2.7. Cronbach alpha for this sample was .51.

Hospital Anxiety and Depression Scale (HADS ((Zigmond & Snaith, 1983)): A 14-item self-report questionnaire developed to assess anxiety and depression. The clinical cut off for each scale (anxiety and depression) is 10. Cronbach alpha for this sample was .92

Autism Quotient 10 (AQ-10 ((Allison et al., 2012)): A short version of the Autism Quotient, used to assess autistic characteristics. The clinical cut-off is six or above. Cronbach alpha for this sample was .17.

Obsessive Compulsive Inventory (OCI-R, ((Foa et al., 2002)): An 18-item scale used to assess levels of distress caused by obsessions and/or compulsions in adults. The clinical cut-off for this measure is 21. Cronbach alpha for this sample was .95.

Children's Obsessive Compulsive Inventory (CHOCI,((Shafran et al., 2003)): A 44-item measure assessing compulsive and obsessive symptoms in children. A total score of 17 and above is considered to be clinically significant. Cronbach alpha for this sample was .94.

Social Anhedonia Scale (SAS, ((Chapman et al., 1976)): A 40-item scale used to assess social anhedonia (diminished interest or pleasure in most or all social activities, (Tchanturia et al., 2012a) A score of 12 or above indicates functionally impairing social anhedonia (Pelizza & Ferrari, 2009). Cronbach alpha for this sample was .36.

Detail and Flexibility Questionnaire (DFlex, ((Roberts et al., 2011)): A 24-item used to examine cognitive rigidity and attention to detail. Clinical significance is placed on scores of 53 and above on the cognitive rigidity subscale and 44 and above on the attention to detail subscale. Cronbach alpha for this sample was .83.

Work and Social Adjustment Scale (WSAS, ((Mundt et al., 2002)): A 5-item measure used to assess the extent to which a given problem has affected one's daily functioning. A score of 20 and above is associated with clinical significance. Cronbach alpha for this sample was .96

7.2.3 Procedure

While viewing each film clip, participants' faces were recorded with their knowledge and agreement. Following the positive and negative film clip, participants completed the positive and negative affect scale.

7.2.4 Data analysis

The normality of each of the outcome variables for the entire sample was assessed. Each of the outcome variables for the FACES data was positively skewed and log transformations were unable to normalize the data. Therefore non-parametric Mann-Whitney U tests were employed to assess group differences. As with other studies using FACES, Spearman's Ro correlation analysis revealed significant correlations between all of the FACES outcome variables. Therefore frequency of positive emotion and frequency of negative emotion were used as the primary outcome variables to assess emotion expression.

Sub-analyses were conducted within the AN group using Spearman's Ro correlation analysis to assess for associations between frequency of emotion expression and demographic and clinical characteristics. Due to the testing of multiple variables, we used a more conservative significance level of 1%, to minimise Type I errors.

7.3 Results

Table 1 displays demographic information for both AN and HC groups. As expected there were significant differences between the AN and HC groups in BMI and %IBW, with the AN group being significantly lower. The AN group also scored significantly higher on all clinical self-report measures.

	AN (N=66)	HC (N=75)	p
Age	20.06 (7.26)	19.85 (7.09)	.86
BMI (adults>18yrs, AN= 31, HC=38))	15.43 (1.41)	21.21 (2.09)	<.001
%IBW (young people<18yrs AN=36, HC=39)	80.53 (6.89)	100.55 (8.12)	<.001
Years of education			.54
Age of onset	15.62 (5.06)	-	-
Illness duration year (>18 years)	7.93 (6.44)	-	-
Illness duration years (<18 years)	1.68 (1.20)		
EDE-Q Global	3.78 (1.61)	1.00 (.77)	<.001
AQ-10	3.90 (2.23)	2.30 (1.59)	<.001
HADS Depression	9.65 (4.82)	1.73 (1.66)	<.001
HADS Anxiety	12.80 (5.15)	4.59 (2.47)	<.001
DFlex attention to detail	46.07 (12.62)	34.43 (8.39)	<.001
DFlex Cognitive rigidity	52.86 (15.90)	34.31 (9.11)	<.001
SAS	16.56 (8.83)	6.97 (4.61)	<.001
WASAS	22.73 (11.37)	.58 (2.46)	<.001

BMI=Body Mass Index (kg/m2); %IBW= Percentage ideal body weight; EDEQ Global= Eating Disorder Examination Questionnaire Global Scale; AQ-10= Autism Quotient 10; HADS=Hospital Anxiety and Depression Scale; OCI-R= Obsessive-Compulsive Inventory-Revised; DFlex= Detail and Flexibility; SAS= Social Anhedonia Scale; WASAS= Work and Social Adjustment Scale.

TABLE 1: Participant demographics for study 5

7.3.1 Emotion expression: FACES

Table 2 displays the medians and interquartile ranges for the frequency of emotion expression and amount of times each group look away during each clip, as well as the means and standard deviations for the PANAS. Mann-Whitney U test revealed that the AN group produced significantly less positive emotions during the positive clip, compared to the HC group. There were no differences in the amount of negative emotions expressed during the positive film clip. There were also no differences in the amount of times each group looked away from the positive clip. There were no significant differences in the amount of positive or negative emotions expressed by each group during the negative film clip. The AN group looked away from the negative clip significantly more times that the HC group.

Emotion expression				
	Median & IQR		P	
	AN (N=66)	HC (N=75)		
Positive clip Positive emotion frequency	3.0 (0.0-9.0)	6.3 (2.1-11.8)	<.01**	
Positive clip Negative emotion frequency	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.80	
Positive clip looking away	1.0 (0.0-3.6)	0.8 (0.0-2.4)	.39	
Negative clip Negative emotion frequency	0.0 (0.0-1.5)	0.0 (0.0-1.5)	.73	
Negative clip positive emotion frequency	0.0 0.0-0.0	0.0 (0.0-0.0)	.51	
Negative clip looking away	4.0 (1.37-7.5)	2.0 (0.0-4.0)	<.01**	
PANAS				
	Transformed means & SDs		p	Cohen's *d*
	AN (N=66)	HC (N=75)		
Positive clip positive scale	1.0 (0.30)	1.1 (0.25)	.09	0.37
Positive clip negative scale	0.5 (0.43)	0.33 (0.35)	<.01**	0.44
Negative clip negative scale	0.87 (0.38)	0.70 (0.31)	<.01**	0.55
Negative clip positive scale	0.65 (0.30)	0.64 (0.87)	.89	0.02

**Significant at 0.01; IQR= Interquartile range; PANAS= Positive and Negative Affect Scale

TABLE 2: Emotion expression and PANAS outcomes.

7.3.2 Subjective emotion: PANAS

The AN group reported feeling the same levels of positive emotions as the HC group on the PANAS. The AN group also displayed emotional incongruence, as they reported feeling significantly more negative emotions on the PANAS during the positive clip, compared to the HC group. In addition, the AN group reported significantly higher levels of negative emotions on the PANAS during the negative clip, compared to the HC group.

7.3.3 Correlates of emotion expression within the AN group

Additional analyses were conducted within the AN group to examine the associations between the frequency of emotion expression and clinical/ self-report measures. The results of the correlation analysis are presented in table 3. Reduced positive emotion expression was associated with the following clinical variables: lower BMI and work and social adjustment; and higher depression, autistic traits, obsessive-compulsive symptoms, social anhedonia. The frequency of negative emotion expression was not associated with any clinical variables. Age was not associated with either of the emotion expression variables.

	Frequency positive emotion, positive clip	Frequency negative emotion, negative clip
Age (years)	.023	-.030
BMI (z score)	.317**	.042
Age of onset	-.033	-.120
Illness duration	.097	.069
EDE-Q global	-.345**	-.072
HADS Anxiety	-.165	-.140
HADS depression	-.284**	-.176
AQ-10	-.223*	.083
OCD (z score)	-.232**	.130
SAS	-.219*	-.115
WASAS	-.204*	-.142
DFLEX Attention to detail	-.119	-.178
DFLEX Cognitive rigidity	-.175	-.147

*Significant at 0.05; **Significant at 0.01
BMI=Body Mass Index (kg/m2); EDEQ Global= Eating Disorder Examination Questionnaire Global Scale; AQ-10= Autism Quotient 10; HADS=Hospital Anxiety and Depression Scale; OCD= Obsessive Compulsive Disorder; SAS= Social Anhedonia Scale; WASAS= Work and Social Adjustment Scale; DFlex= Detail and Flexibility.
TABLE 3 : Spearman's Rho correlations between emotion expression and demographic and clinical variables.

7.4 Discussion

The aim of this study was to investigate emotion expression in a group of patients with AN across a wide age spectrum, and to investigate the clinical and demographic correlates associated with reduced emotion expression.

Our findings are in agreement with the previous exploratory studies of Davies et al. (2011) and Rhind et al. (2014), whereby individuals with AN displayed significantly less positive emotion expressions during the positive clip, despite reporting feeling the same levels of positive emotion subjectively. We also found that the AN group looked away from the negative film clip significantly more than the HC group, supporting the notion of intolerance of the negative stimuli and an attempt to avoid the negative affect that it may evoke (Wildes, Ringham, & Marcus, 2010).

In addition to these findings, our study also found that there were no differences between the groups in the frequency of emotion expressivity during the negative film clip, whereas the AN group reported significantly higher levels of negative emotions subjectively compared to HC. Conversely, the AN group reported significantly higher negative feelings during the positive film, but this was not reflected in the amount of negative emotion expression observed. Emotion incongruence was also observed within the AN group, whereby they reported significantly higher levels of negative emotions during the positive film clip.

These findings provide further support for reduced positive emotion expression in children, adolescents and adults with AN, providing additional empirical support to the literature in the context of social communication difficulties in patients with AN. The findings from this study suggest that although individuals with AN may experience an intense emotion, such as happiness or joy, they are unable to signal that emotion to the observer. Being able to signal one's own emotional state or intent is essential for effective everyday social communication, for example being able to smile to signal amusement or willingness to interact. Therefore difficulties with accurately signaling one's own emotional state could carry negative consequences for everyday social situations, and may contribute to the difficulties individuals with AN report in social settings, such as maintaining friendship groups (Doris et al., 2014). For example, expressing fewer positive emotions could limit

opportunities for positive social experiences and result in social isolation (Fredrickson, 2010). Furthermore, such difficulties could also negatively impact on treatment engagement, as it is hard for a therapist to calibrate how their patient may be feeling based on the limited feedback they are observing. This may in turn impact on the therapeutic alliance between patient and therapist, a factor shown to be very important to the effectiveness of psychological therapies (Simos, 2002).

In addition to this, emotional incongruence as observed in this study can make social interaction even more problematic. Experiencing the opposite emotion may mean that the individual is not interpreting the social situation in the same way as most others. This would make responding to complex social situations appropriately incredibly difficult. Furthermore, social abilities such as mentalising and empathising could also be compromised by this, as 'putting yourself in someone else's shoes' is very difficult if you often feel the opposite way to most people.

The high levels of negative emotions during a positive clip in this study could be due to a hyper-sensitivity towards observing an embarrassing scene. Symptoms of social anxiety are known to occur at a high rate in individuals with AN (Kaye et al., 2004). The positive film clip depicts a humorous scene whereby a priest mispronounces his words during a wedding ceremony. The AN group could find this scene aversive and rather anxiety-provoking to watch, tying into symptoms of social anxiety. Social anxiety was not specifically measured within this study and therefore the associations between it and this experimental stimuli cannot be tested. It is also important to note the high levels of self-reported anxiety and depression by the AN group in this study, therefore the emotional incongruence could reflect the high levels of baseline anxious and depressive symptomatology in this group.

Sub-analyses within the AN group revealed that lower levels of positive emotion expressivity were associated with more severe clinical symptoms such as lower BMI and higher eating disordered psychopathology, depression, OCD, autistic traits, social anhedonia and work and social functioning. This may suggest that individuals with poor emotion expression represent a particularly severe group with more socio emotional difficulties, who may not respond well to standard psychological treatments. This finding, taken together with previous evidence of raised levels of autistic traits and social anhedonia, as well as difficulties with work and social

adjustment in AN populations (Baron-Cohen et al., 2013; Hambrook et al., 2008; Tchanturia et al., 2012a; Tchanturia et al., 2013c) suggests that developing treatments that consider and directly target these underlying mechanisms, in addition to overt eating disorder pathology, could result in improved outcomes for AN. Qualitative studies suggest that the need for treatments addressing emotional processing difficulties are recognised by patients, clinicians and carers (Kyriacou, Easter, & Tchanturia, 2009).

At present there are several treatment innovations addressing emotional processing in eating disorders for example: a manualised outpatient treatment for AN, including a social emotional module (Schmidt et al., 2012); Cognitive remediation and emotion skills therapy (CREST) in individual and group formats (Money et al., 2011; Tchanturia et al., 2014a); Emotion Acceptance Behavior Therapy (EABT) for Anorexia Nervosa's main focus is to increase awareness and help to cope with emotions (Wildes & Marcus, 2011); and Radically Open-Dialectical Behavior Therapy (RO-DBT) (Lynch et al., 2013).

Evidence gathered from neuroimaging studies has revealed different patterns of activation during the processing of positive emotional stimuli in AN groups in comparison to the HCs (Fonville, Giampietro, Surguladze, Williams, & Tchanturia, 2014b; Friederich et al., 2006). These studies highlight that different biological mechanisms may be at play for individuals with AN when processing social stimuli. Such findings provide support for the development of treatments not only focusing on emotion processing, but that in particular utilising positive psychology in ED to directly target this underlying process (Tchanturia et al., 2015). These interventions could improve social functioning and positively impact the outcome of other psychological treatment for AN. It is important for future research in emotion expression to incorporate neuroimaging, to delineate the exact neural underpinnings of reduced emotion expression in AN.

Whether such difficulties with emotion expression may be a consequence of starvation or not should also be acknowledged. There is currently one study in the literature that has examined emotion expression in a recovered group (Davies et al., 2013). Although they did not find any significant differences, there was a tendency

for lower emotion expressivity in the recovered group and they appeared to show an intermediate profile between the AN and HC groups. Such non-significance may be a result of the recovered group being underpowered in this study. However, these preliminary results suggest that reduced emotion expression may pre-date the onset of AN and then possibly be worsened by starvation.

Interestingly, in the present study, the age of the participants had no association with emotion expression. This finding is at odds with findings from other areas of socio-emotional processing in AN, which found that being of a younger age and having AN predicted poorer emotion recognition when measured using the body motion paradigm the 'pointlight walkers' (Lang et al., 2015a).

The finding that age was not associated with poor emotion expression in the present study is a positive one, as although it is preliminary, it could suggest that some areas of emotion processing, such as emotion expression, maybe preserved in individuals with AN and more susceptible to the effects of long-term starvation and ED pathology (Davies et al., 2013). One possible explanation for this finding could be due to this study group consisting only of females. There is evidence that both gender and verbal IQ are protective factors against social communication difficulties in children and adolescents (Skuse et al., 2009). As the group in the present study was female, and individuals with AN typically have an higher than average IQ (Lopez et al., 2010), this could explain why age was not associated with reduced emotion expression.

The strengths of this study are its large sample size and its inclusion of a spectrum of both age and severity in AN. However, there are limitations such as using of stimuli that had not been validated for child and adolescent populations.

7.5 CONCLUSIONS

In summary the present study replicated the findings of previous studies, demonstrating that individuals with AN display altered emotion expression. Lower levels of emotion expression were associated with some clinical symptoms, suggesting that these individuals could represent a particularly challenging group, which could benefit from tailored treatments that directly target emotion processing.

CHAPTER 8

GENERAL DISCUSSION

8.1 Overview

This thesis consists of a series of studies aimed at improving our understanding of underlying mechanisms that are likely to be important in both the pathogenesis and maintenance of Anorexia Nervosa (AN).

Through the use of literature reviews, experimental studies and clinical pilot studies, this research aimed to add to the existing knowledge base regarding neuropsychological and socio-emotional processing in children and adolescents with AN, and translate these empirical findings into clinical practice by defining treatment targets and increasing the limited treatment options available for AN.
This final chapter will aim to summarise the key findings that have resulted from these studies and synthesise them with the existing literature. The implications, strengths and limitations of the studies will be considered, followed by an overall conclusion.

8.2 Summary of key findings

8.2.1 STUDY 1: Do children and adolescents with Anorexia Nervosa display inefficient cognitive processing?

This study aimed to investigate the neuropsychological characteristics of children and adolescents with AN by comparing their performance on measures of both set shifting and central coherence to HC children and adolescents. This study found significant differences between the groups on the Wisconsin Card Sorting Test (WCST), whereby children and adolescents with AN made significantly more perseverative errors with medium effect sizes.

The AN group also scored significantly lower on the style index and the central coherence index of the Rey Osterrieth Complex Figures Test (ROCFT) compared to the HC group. The order index of the ROCFT was approaching significance with a small effect size (d=0.36) with the AN group demonstrating lower scores. Similarly, there was also a trend towards significance on the Fragmented Pictures Task (d=0.38), whereby the AN group took a longer amount of time to correctly identify the pictures. These scores suggested an inefficient processing style in the AN group, characterised by a more inflexible thinking and less holistic processing style. Within the AN group, inefficient cognitive processing was not associated with any clinical or demographic variables, and there were no differences in cognitive processing style between those taking psychopharmacological medications and those who were medication free.

Overall, the findings of this study suggest that children and adolescents with AN display a similar inefficient cognitive profile to adults with AN, and that this processing style could be an underlying trait of AN.

8.2.2 STUDY 2: Is inefficient cognitive processing in Anorexia Nervosa a familial trait? A neuropsychological pilot study of mothers of offspring with diagnosis of Anorexia Nervosa.

Study 2 set out to investigate set shifting and central coherence in unaffected mothers of offspring with AN. Data were collected on the WCST, the ROCFT and the

FPT task from 21 unaffected mothers of offspring with AN and 20 mothers of HC children. There were significant differences across all of the neuropsychological measures, with the unaffected mothers displaying a more inflexible thinking style on the WCST and lower levels of global processing on ROCFT and the FPT.

The results of this study further support the notion that these characteristics are familial, and also add further evidence to suggest they may represent an inherited vulnerability in AN.

8.2.3 STUDY 3: Acceptability and feasibility of self-help Cognitive Remediation Therapy for Anorexia Nervosa delivered in collaboration with carers: A qualitative preliminary evaluation of a pilot study.

Study 3 described the first attempt to assess the feasibility and acceptability of a self-help module of Cognitive Remediation Therapy (CRT) to be delivered in collaboration with carers. Following a short training session, six families (mother-daughter pairs) underwent a six-week self-help intervention whereby they used an amended version of the clinician's CRT manual in a collaborative fashion (please see www.katetchanturia.com for a version of the manual). Feedback regarding the feasibility and acceptability of CRT in this modality were collected from both individuals with AN and their families via a qualitative interview and neuropsychological measures were also administered pre and post intervention.

The feedback gathered from the qualitative interview suggested that self-help was an effective and acceptable form of delivery for CRT, with both AN participants and families describing a number of benefits to this modality. Feedback regarding the involvement of family members or carers in this treatment was also generally positive.

There were also improvements in neuropsychological function post intervention for each AN participant and their carer, but due to the small sample sizes in this study these results must be interpreted with caution. Taken together, these findings provide preliminary evidence to suggest that self-help CRT in collaboration with carers is an effective and acceptable form of treatment.

8.2.4 STUDY 4: Exploring Emotion Recognition in Adults and Adolescents with Anorexia Nervosa Using a Body Motion Paradigm

Study 4 provided an empirical study of emotion recognition through body motion with adults and children and adolescents with AN. This study aimed, firstly, to investigate the ability of individuals with AN to discern different emotional states through body language and, secondly, to investigate the impact of age on this ability.
The results revealed significant differences between the AN and HC groups, whereby the AN group were significantly worse at identifying sadness. Further analyses of the data revealed that children and adolescents with AN performed worse in this task overall. These findings provide evidence of subtle difficulties in recognition of sadness through body motion in AN, and also the first evidence of particularly poor performance in children and adolescents with AN, suggesting a possible interaction between starvation and the typical developmental trajectory of such faculties.

8.2.5 STUDY 5: Emotion expression and associated clinical factors in children, adolescents and adults with Anorexia Nervosa.

This study aimed to investigate facial emotion expression across the age range (11-47 years) in AN. The study employed stimuli designed to evoke positive and negative emotion expression, and facial emotion expressivity were coded using the Facial Expression Coding System (FACES). Subjective ratings of emotional state were collected using the Positive and Negative Affect Scale (PANAS).
The findings of this study demonstrated altered emotion expression in the AN group, whereby they displayed significantly less positive facial expression during the positive clip, despite subjectively reporting feeling the same levels of positive emotions as the HC group. The AN group also reported experiencing significantly higher levels of negative emotions during the positive clip. There were no significant differences in the frequency of negative emotions expressed during the negative clip between the AN and HC group. However, the AN group did subjectively report experiencing a significantly higher level of negative emotion on the PANAS.

Further analyses within the AN group revealed that lower levels of emotion expression were associated with a number of clinical correlates. These results suggest a particular difficulty with the expression of positive emotion in AN, and that individuals with poorer emotion expression could represent a more clinically and socially impaired group. The age of the participants in the AN group was not associated with poorer emotion expression.

8.3 Synthesis with existing literature

8.3.1 Neuropsychological processing in children and adolescents with AN

The previous literature regarding set shifting abilities in children and adolescents with AN was limited and the findings were inconsistent. A meta-analyses of studies employing the WCST and the Trail Making Task (TMT) found no significant differences in performance between AN or HC groups on either task, however there was a general tendency for AN groups to show a slightly more perseverative style. Studies using other neuropsychological measures of set shifting such as the Groton Maze Learning Task (Cogstate program. Available at: http://cogstate.com/), and the Brixton task (Burgess & Shallice, 1997), the Intra/Extra Dimensional shift task (Downes et al., 1989), colour word interference (Lezak et al., 2012), the verbal fluency test (Lezak et al., 2012), the category learning test (Filoteo et al., 2005) and the visual set shifting test (De Sonneville, 2000) have produced mixed results, with some studies finding significant differences between AN and HC groups (Frampton et al., 2012; Hatch et al., 2010b), and some reporting no significant findings (Búhren et al., 2012; Fitzpatrick et al., 2012; McAnarney et al., 2011; Shott et al., 2012). Similarly, the available literature regarding central coherence in children and adolescents with AN was limited and demonstrated inconsistent findings (Kjaersdam Telléus et al., 2014; Rose et al., 2014).

It was postulated that the inconsistency of these findings in the neuropsychological profile of children and adolescents could be due several methodological constraints within the current literature, and as there was a tendency for a more inflexible thinking style and less holistic processing within the AN group (albeit non-significant), this could suggest that significant differences between the groups could be found if such study limitations were addressed.

For example, although Búhren et al. (2012) did not finding significant differences between children and adolescents with AN and HC children and adolescents in their main outcome measure of cognitive flexibility (an accuracy score), they did find significantly longer reaction times by the AN group during trials where a set shift was required. These results are suggestive of an inflexible thinking style in the AN group, leading the authors to postulate that other possibly more sensitive set shifting paradigms, such as the WCST, may have exposed group differences further.

With this in mind the present study was designed to address these limitations, by recruiting a large sample and employing robust neuropsychological tasks that had been informed by prior reviews of the literature. Using this methodology we found small-medium sized differences between the AN and HC groups, with children and adolescents with AN displaying an inefficient processing style, characterised by a more inflexible cognitive style with lower levels of global processing.

8.3.2 Neuropsychological processing in unaffected mothers of AN offspring

Study 2 found significant differences between unaffected mothers of offspring with AN and mothers of HC offspring across measures of set shifting and central coherence. These findings are consistent with the previous literature regarding unaffected family members, suggesting that inefficient cognitive processing is a familial trait.

The previous literature had highlighted higher levels of inefficient cognitive processing in unaffected first-degree family members by showing that unaffected sisters of those with AN displayed a more inflexible thinking style and lower levels of global processing compared to HCs. One study included a mixed sample of both unaffected sisters and mothers, also finding poorer set shifting in the unaffected relatives in comparison to HCs. A twin study also demonstrated a likely genetic component with high concordance rates of inefficient set shifting in monozygotic and dizygotic twins. The present study builds on this literature providing further evidence that inefficient cognitive processing is a familial trait in AN.

It is important to compare these findings with findings from the wider psychiatric field. The strongest evidence of a genetic underpinning of these traits can be seen in the autism literature (Happé, 2013; Hill, 2004). However, the evidence of inefficient cognitive processing in unaffected relatives in other psychiatric disorders such as OCD and Schizophrenia was mixed and inconsistent (Cavedini et al., 2010; Delorme et al., 2007; Snitz et al., 2006). In comparison, the findings from the present study along with the existing AN literature provide stronger evidence for the familial nature of these characteristics in AN. Consistent evidence of inefficient cognitive

processing across a number of neuropsychological measures (Galimberti et al., 2013; Holliday et al., 2005; Roberts et al., 2010), which when taken in combination with the results of twin studies (Kanakam et al., 2013), could suggest that they are an inherited vulnerability in AN and could possibly represent an endophenotypic trait in AN.

8.3.3 Socio-emotional processing in children and adolescents with AN

The existing literature concerning socio-emotional processing in children and adolescents with AN was small. The findings from studies 4 and 5 of this thesis are in line with the available literature, providing further evidence of socio-emotional processing difficulties in children and adolescents with AN. They also provide novel evidence that extends beyond the existing literature.

A main finding from study 4 was that individuals with AN were significantly worse at recognising sadness through a body motion paradigm. Although these difficulties were subtle in the present study, they are in line with previous findings concerning the recognition of sadness. Zucker et al. (2013) also reported significant differences in the recognition of sadness using the same emotion recognition task. Furthermore, previous studies have also found difficulties in recognising sadness through facial emotions in AN (Castro et al., 2010; Kucharska-Pietura et al., 2004).

Study 4 was the first study to examine emotion recognition using a body motion paradigm in a younger AN population, and added to the existing literature with the novel finding that children and adolescents with AN demonstrated the poorest recognition of sadness overall. Although no studies have previously investigated emotion recognition through body motion in children and adolescents, these findings do fit with the literature regarding facial emotion recognition, which have demonstrated poorer emotion recognition abilities in children and adolescents with AN (Zonnevijlle-Bendek et al., 2002).

The findings from Study 5 regarding facial emotion expression in adults and children and adolescents with AN are largely consistent with the previous literature. Davies et al. (2011) reported that in comparison to HCs individuals with AN produced

significantly less positive and negative facial expressions in response to positive and negative film clips, whilst reporting subjectively feeling the same levels of positive emotion and higher levels of negative emotion. Furthermore, the AN groups looked away from the negative clip significantly more than the HC group. Rhind et al. (2014) replicated these findings in children and adolescents. The present study found that individuals with AN produced significantly less positive emotion expressions during the positive clip, whilst reporting the same levels of positive emotions subjectively. The finding that the AN group looked away significantly more during the negative clip was also replicated.

However, the present study found that there were no differences in the frequency of negative facial emotions produced during the negative clip between the groups, but the AN group did report feeling significantly higher levels of negative emotions. Additionally, emotional incongruence was observed, with the AN group reporting significantly higher levels of negative emotions during the positive clip. The emotional incongruence may have been due to a hyper-sensitivity towards the comical but potentially embarrassing scene depicted in the positive clip, which may have provoked symptoms of social anxiety in the AN group. Alternatively, it may reflect higher levels of baseline anxiety and depression in the AN group.

8.4 IMPLICATIONS

The results from the series of studies presented in this thesis have implications for our understanding of both the aetiology and maintenance of AN, as well as implications for its treatment.

8.4.1 Implications for the understanding of the aetiology and maintenance of Anorexia Nervosa

8.4.1.1 The neuropsychology of AN

There is currently a wealth of research consistently demonstrating a specific neuropsychological processing profile in adults with AN, characterised by inefficient set shifting and weak central coherence (Harrison et al., 2011; Lopez et al., 2008b; Roberts et al., 2007; Tchanturia et al., 2012b). This profile is also present in an attenuated form in recovered individuals (Lindner et al., 2014; Roberts et al., 2010), and there is evidence of its presence in unaffected relatives to a higher degree than the healthy population (Roberts et al., 2010, 2013). These findings have led to the postulation that inefficient cognitive processing could be an endophenotypic trait of AN.

However, at the time this thesis was conceived the literature regarding the neuropsychology of child and adolescent AN was limited and firm conclusions regarding the processing style of children and adolescents with AN could not be made. Elucidating this profile in children and adolescents would have important implications for the status of these characteristics as stable traits as the effects of long-term starvation should be less pronounced in younger individuals with shorter illness durations. Furthermore, given the elevated risk for the development of AN in adolescence, research aimed at improving our understanding of potential causal and maintenance factors during this period is of great value.

The findings from study 1 of significantly poorer set shifting abilities and lower levels of global processing add strong evidence to support the presence of inefficient cognitive processing in children and adolescents with AN, and the results are similar to the profile observed across a number of adult AN studies using the same neuropsychological measures (Harrison et al., 2011; Tchanturia et al., 2012b).

Furthermore, such inefficient cognitive processing was independent of disorder severity (as measured by %IBW and length of illness), as well as other clinical factors such as anxiety and depression. These findings therefore carry important implications for our understanding of the aetiology of AN as they provide further support that such characteristics are likely to be underlying traits contributing to the pathogenesis and maintenance of AN.

Figure 1 presents a radar chart depicting the effect sizes found in the present study against the effect sizes of the large adult studies using the same methodology (WCST=Tchanturia et al. 2012; FPT=Harrison et al. 2011; ROCFT=Lopez et al. 2008).

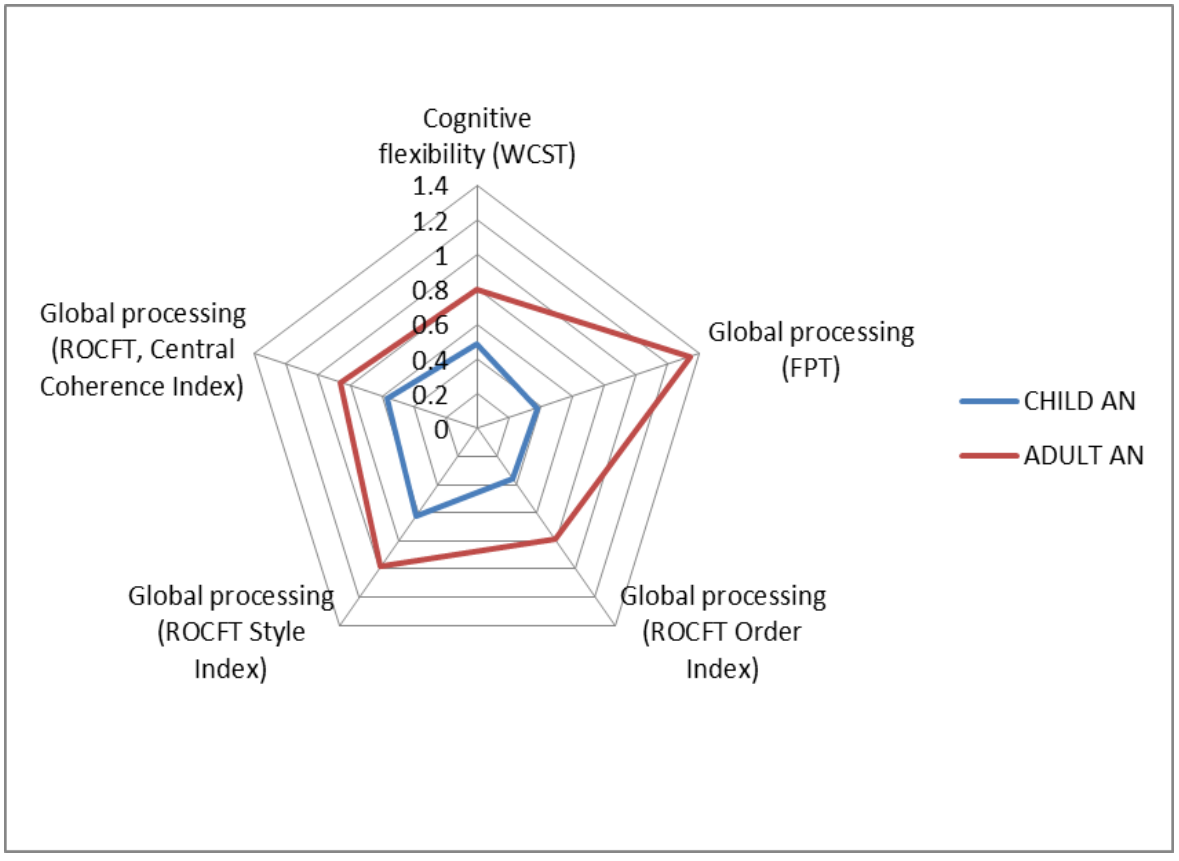

Figure 1: Radar chart of effect sizes (Cohen's d) from the neuropsychological tasks for the children and adolescents in study 1 and adult AN studies.

The graph demonstrates that whilst small to medium effect sizes were observed in the present study with children and adolescents, medium to large effect sizes are being observed across the same neuropsychological tasks in the adult AN population. This comparison provides further evidence that although these

characteristics are likely to be underlying traits predating the onset of the disorder (as demonstrated in the present study in a group of individuals with short illness durations), illness characteristics such as chronicity and severity are also likely to worsen these characteristics further, demonstrated by the larger effect sizes in the adult AN studies.

Furthermore, it has been suggested that whilst a processing bias towards details may be an underlying trait in AN, poor global processing may in fact be more related to starvation effects (Treasure & Schmidt, 2013), leading to weak central coherence in more severe and chronic cases. Figure 1 provides support for this notion, with smaller effect sizes for global processing tasks such as the FPT and order index of the ROCFT being observed in the child and adolescent group, in comparison to the exaggerated profile in adult AN groups.

Such findings are in line with the staging model of AN (Treasure et al., 2014), suggesting that higher levels of these traits are vulnerability markers and are present in the prodromal and early stages of AN. As illness duration increases, neuroprogressive features such as biological brain changes and neurological scars develop as a consequence of starvation and malnutrition. The underlying traits of cognitive inflexibility and bias towards detail are worsened as a consequence, and therefore are accentuated in adult AN populations. These exacerbated traits are likely to cause further treatment complications and contribute to the poorer prognostic outcomes associated with severe and enduring AN.

Differences in brain maturation between children and adolescents with AN and adults with AN should also be acknowledged. Cognitive control functions are thought to be modulated by fronto-striatal brain circuits that continue to mature into late adolescence and adulthood (Sowell et al., 2001). These differences in brain structure and function could also in part, explain the differences in cognitive profile between children and adolescents with AN and adults with AN.

Study 2 demonstrated the presence of both inefficient set shifting and lower levels of global processing in unaffected mothers with offspring with AN, providing further evidence of the familial nature of these characteristics. These findings have further implications for our understanding of familial cognitive style as both a vulnerability

and a maintaining factor in AN. Figure 2 displays a radar chart depicting the effect sizes from study 2 with effect sizes from the children and adolescents with AN in study 1 of this thesis, and adult AN studies using the same methodology (WCST=Tchanturia et al., 2012; FPT=Harrison et al., 2011; ROCFT=Lopez et al., 2008). Although the data from this study is preliminary, the figure demonstrates that the effect sizes obtained from the unaffected mothers in study 2 are similar to the effect sizes being observed in adult AN populations. Unhelpful cognitive styles within families, such as inefficient set shifting and lower levels of global processing are likely to negatively impact on the responses of carers to ED behaviours. An inflexible thinking style may produce a more ridged parental style, making adjustment to the illness more difficult, whereas a detailed focus bias may make it more difficult to see the wider context of the problem.

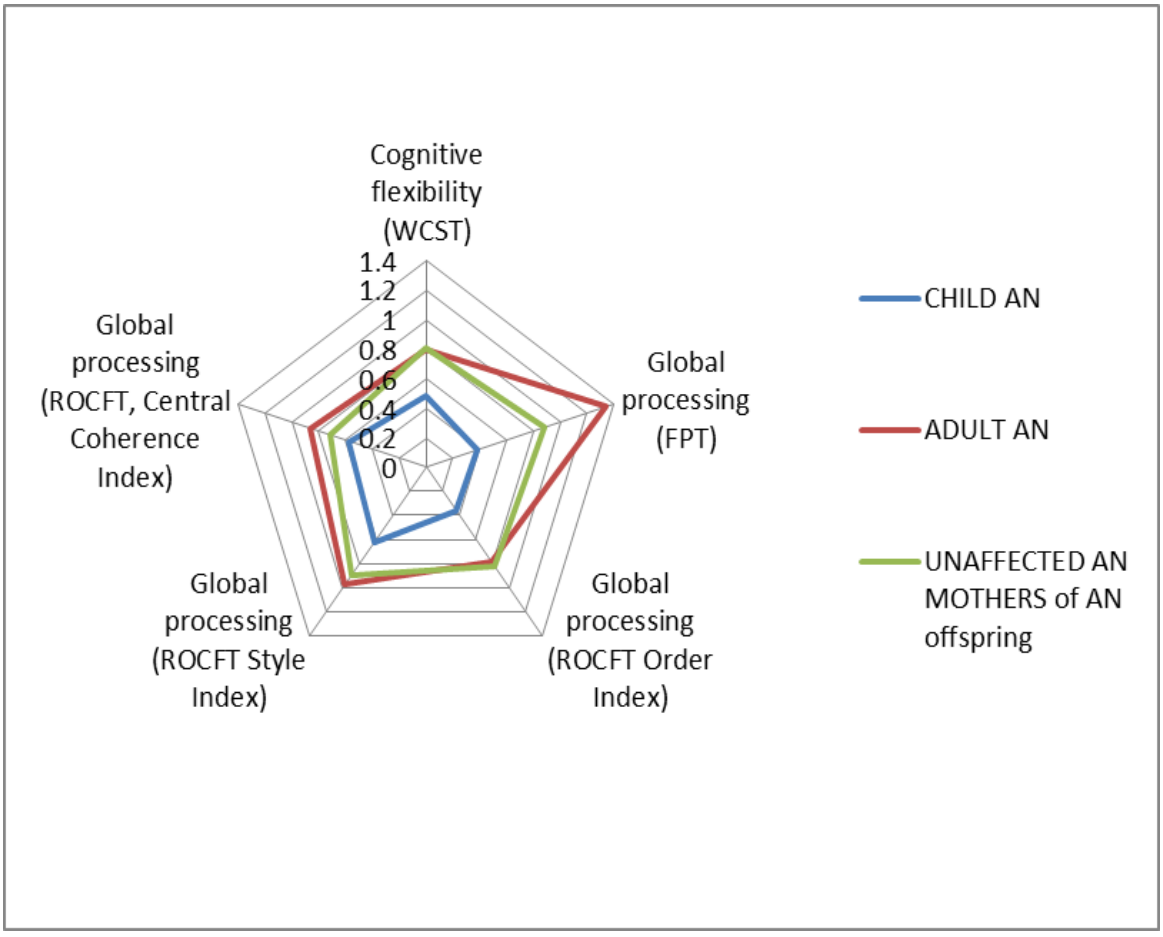

Figure 2: Radar chart of neuropsychological effect sizes for unaffected mothers in study 2, children and adolescents in study 1 and adult AN studies.

Taken together, the findings regarding the presence of such characteristics in younger samples and the familial nature of these traits add to the evidence base suggesting that inefficient cognitive processing may represent an underlying trait and an inherited risk factor in AN. This data adds tentative evidence that they may be endophenotypic traits for AN.

Elucidating potential endophenotypes of AN also has implications for genetic research into the disorder. As endophenotypes are believed to lie somewhere on the pathway between the genetics and the phenotypic expression of a disorder, such findings could help aid the search for candidate gene studies.

8.4.1.2 Socio-emotional processing in AN

The results of these studies provide additional evidence of the importance of socio-emotional difficulties as predisposing and maintaining factors in AN.

The findings from study 4 of difficulties in emotion recognition through body motion, albeit subtle and specific to sadness, are in line with findings from other areas of emotion recognition (Castro et al., 2010; Kucharska-Pietura et al., 2004; Pollatos et al., 2008; Zucker et al., 2013). Difficulties in recognition of sadness in others can lead to problematic social interactions, making responding appropriately to others who may be in distress difficult. Consequently, this could lead to social isolation and withdrawal, and serve to maintain ED pathology further.

Furthermore, the findings that altered emotion expressivity was associated with a range of clinical symptoms, such as lower BMI and social functioning and higher ED and other psychopathology, further supports the notion that disrupted socio-emotional processing is a prominent factor in the maintenance of symptoms associated with severe and chronic AN, and is likely to complicate treatment. These findings suggest that although altered emotion expressivity is likely to be present in early onset and early stage AN, it is likely to be further negatively impacted by starvation, effecting individuals in the severe and enduring stages of AN more profoundly.

This is the first study of its kind to demonstrate poorer performance by children and adolescents with AN in a body motion task, and these findings could shed more light on how starvation may exacerbate social difficulties and cause disruption to the

typical developmental trajectory of such functions. They raise the interesting question of whether this poor performance could be due to a pre-existing underlying difficulty in emotion recognition interacting with starvation effects during a critical period of social cognitive development in the brain, further disrupting the typical trajectory. More work is needed, possibly incorporating brain imaging with younger populations to investigate this postulation further.

Taken together, these findings may suggest slightly different socio-emotional processing profiles may exist between children and adolescents with early onset AN and adults with full or severe and enduring AN. These differences may be reflective of a combination of different developmental trajectories as well as illness severity stages.

8.4.2 Implications for a working aetiological and maintenance model of Anorexia Nervosa.

Figure 3 presents a tentative model of AN based on previous theoretical models, and with the added contribution of how the present study's findings may contribute to our understanding. Based on previous theoretical models (such as the Neurodevelopmental Model (Connan et al., 2003), Cognitive Interpersonal Maintenance Model (Treasure & Schmidt, 2013) and the Stages Model (Treasure et al., 2014)), the model suggests that there are numerous biological and psychosocial risk factors important in the pathogenesis of AN, as well as implicating age and gender as specific risk factors. Like previous models, this model suggests that there is likely to be triggers involved such as a stressful life event, which could potentially start the ED. Existing underlying factors such as inefficient cognitive and socio-emotional processing are likely to not only render certain individuals more susceptible to developing AN, but also serve to maintain it once it has begun. These characteristics are thought to predate the disorder and are likely to be present in the prodromal phase. As evidenced in figure 1 and by the association found in study 5, these characteristics are worsened by starvation effects and therefore present more profoundly across the severity stages of AN, impeding treatment in these sub-groups. Furthermore, poorer socio-emotional processing abilities are also linked to worse social function, further interfering with treatment. Data from the present

study has also strengthened the evidence suggesting that familial inefficient cognitive processing is likely to further maintain ED pathology and hinder recovery (figure 2).

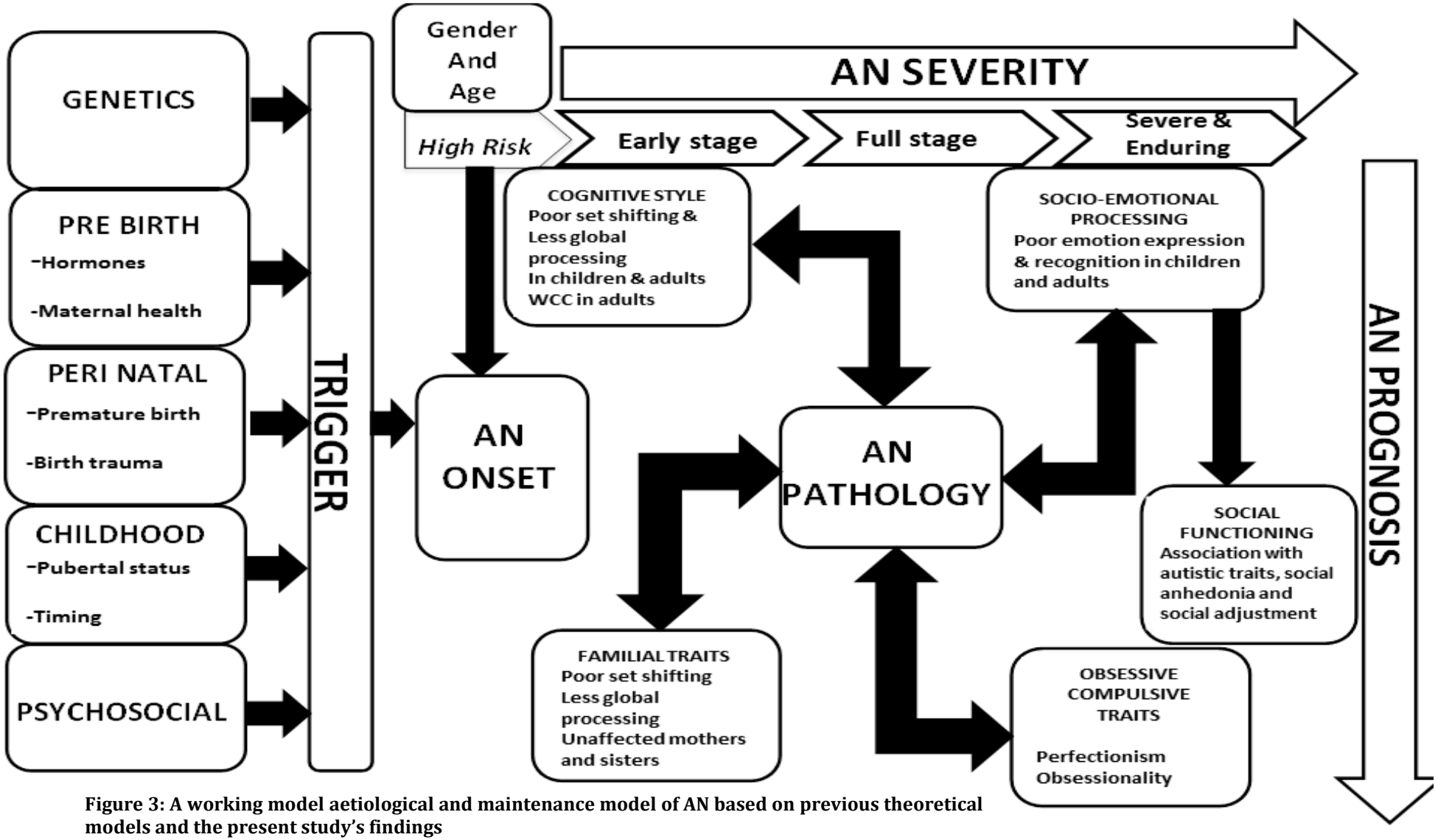

Figure 3: A working model aetiological and maintenance model of AN based on previous theoretical models and the present study's findings

8.4.3 Clinical implications

The findings from study 1 of the existence of inefficient cognitive processing in children and adolescents with AN carry important clinical implications for the treatment of younger populations with AN.

CRT for AN had been developed with the aim of remediating the neuropsychological difficulties observed in the adult AN population (Tchanturia et al., 2013b). There is evidence to suggest improvement in cognitive function following treatment intervention (Brockmeyer et al., 2014; Dingemans et al., 2013; Lock et al., 2013), as well as positive feedback from both patient and therapist populations regarding the acceptability of CRT as a treatment (Abbate-Daga, Buzzichelli, Marzola, Amianto, & Fassino, 2012; Easter & Tchanturia, 2011; Whitney, Easter, & Tchanturia, 2008). There are also preliminary studies suggesting its acceptability with children and adolescents (Pretorius et al., 2012; Wood et al., 2011), with it most commonly being used in severe and enduring populations (Tchanturia et al., 2014b). However, until now strong evidence of inefficient cognitive processing in children and adolescents has not been available, and therefore support for a treatment aimed at remediating cognitive inefficiencies has also been lacking.

The findings from this study provide evidence and support for the implementation of CRT with younger populations. In light of these findings and the results from Randomised Controlled Trials (RCTs) of CRT with adults with AN, such implementation with children and adolescents is likely to be beneficial in the remediation of inefficient cognitive processing, and may lead to improvements in the engagement and outcome of other psychological therapies. Furthermore, the apparent intermediate profile of children and adolescents (Figure 1) supports the importance of early intervention treatments in AN. Such treatments could act as protective factors against neuroprogressive characteristics and prevent progression into the more severe and treatment resistant stages of AN.

Several preliminary studies have recently been published that highlight the potential CRT may have in relation to cognitive processing in younger AN populations. Dahlgren et al. (2013) found significant improvements to cognitive functioning, as well improvements to ED and other psychopathology in 20 adolescent females with

AN following a course of individually delivered CRT. Additionally, there were also significant reductions in self- and parental- reported rigidity. Noort et al. (2015) conducted a pilot study assessing short-term effects of CRT on cognition in 20 adolescents females with AN. Cognitive performance pre-and post-treatment was also compared to 20 matched HC female adolescents whom had not undergone the CRT treatment. In comparison to the matched HCs, the AN group showed significant improvements to flexibility. However, there were no improvements to central coherence.

Therefore, the results from the present study in combination with the preliminary evidence of improvements in cognitive functioning following CRT in children and adolescents with AN, provide strong support for the use of CRT in younger populations with AN. Large randomised controlled trials of CRT with children and adolescents with AN are now required to confirm this postulation.

The results from study 2 provide further evidence of the familial nature of cognitive processing and also provide evidence to implicate familial cognitive style as a heritable risk factor as well as a maintaining factor for the disorder. Thinking styles such as high levels of cognitive inflexibility and inability to see the bigger picture within family members caring for individuals with AN may negatively impact on responses, producing maladaptive behaviours that inadvertently serve to sustain the ED.

These findings indicate that including family members in treatments aimed at making patients and families aware of their thinking styles and develop alternative strategies of cognitive processing, could prove beneficial for the treatment of AN, as a reduction in familial inefficient cognitive processing could result in more adaptive coping to ED pathology. Furthermore, figure 2 suggests that unaffected AN mothers may have similar cognitive profiles to adults with AN, and therefore may themselves benefit from involvement in CRT.

The preliminary results from study 3 further support the notion of the inclusion of family members in CRT. This study demonstrated, for the most part, the beneficial involvement of carers in this treatment. Qualitative feedback gathered from both individuals with AN and parents demonstrated numerous benefits including

improvement in relationship between care-giver and offspring, creating a gateway to more emotional problem-solving, as well as reduction in care-giver self-reported depression and anxiety. Care-giver stress and burden within AN is extremely high (Graap et al., 2008; Hibbs, Rhind, Leppanen, & Treasure, 2015; Treasure, Gavan, Todd, & Schmidt, 2003) and therefore treatments that include carers are favourable (Goddard et al., 2011). The results of this study suggest that the inclusion of family members in CRT holds numerous benefits including reduction in both care-giver stress and burden and potential improvements to familial cognitive style, both of which are likely to further maintain the ED.

Study 3 was also the first study in the field of eating disorders to demonstrate that self-help is a suitable and acceptable mode of delivery for CRT for individuals with AN. Although these findings will need to be replicated on a larger scale, the preliminary findings from this study have implications for treatment, in terms of increasing the accessibility of treatment to individuals who may not otherwise have access, for example due to inability to travel to a clinic or lack of available services or trained clinicians. Furthermore, it could speed up the accessibility to treatment by easing pressure on waitlist times.

The findings of these studies also have implications for the long-term sustainability of CRT outcomes. A big challenge in the delivery of CRT is helping patients to continue to break cognitive habits once therapy has finished. Self-help CRT in a family context increases the sustainability and translational value of this treatment by increasing the opportunities for shifting maladaptive thinking patterns and breaking cognitive habits in everyday life with additional support from carers.

AN is a costly disorder to treat (BEAT, 2012) and therefore self-help treatments are a valuable asset to today's health service as they can help to ease economic pressure by requiring less therapist input. Larger studies of the efficacy of self-help CRT including planned health economic evaluation will be required to confirm this.
Although preliminary, the findings of improved neuropsychological functioning post treatment could suggest that treatment of this kind could be beneficial in remediating inefficient processing, and therefore could aid with engagement.

The findings from this thesis have provided further evidence of the importance of socio-emotional processing difficulties in the aetiology and maintenance of AN and therefore also have important clinical implications in regard to developing new treatments that directly target socio-emotional processing.

There are currently a number of treatments that include modules focussing on socio-emotional processing in AN, including MANTRA (Schmidt et al., 2012); CREST (Money et al., 2011; Tchanturia et al., 2014a); Emotion Acceptance Behavior Therapy (EABT) for Anorexia Nervosa (Wildes & Marcus, 2011); and Radically Open-Dialectical Behavior Therapy (RO-DBT) (Lynch et al., 2013). Several key findings from these studies may help to shed light on the most effective ingredients to include as part of such treatment modules.

The findings from study 4 suggest that the difficulties observed in recognising emotions through body language are fairly subtle in AN in comparison to findings in other areas of emotion recognition. These findings could suggest that treatments aiming to improve socio-emotional functioning in AN should place less emphasis on emotion recognition through body language. However, the findings of difficulties in the recognition of sadness through body motion are consistent with findings from other areas of emotion recognition (such as facial emotion recognition), suggesting specific difficulties in the recognition of this particular emotion. It may therefore be important and beneficial for treatments to place emphasis on developing this particular skill in treatment.

The findings from study 4 of particular difficulties in the recognition of sadness for children and adolescents, and the possibility that this could be due to starvation during critical periods of brain maturation, highlight the need for treatments to prioritise social support for younger patients, with the aim of providing early intervention to prevent social withdrawal that is likely to negatively impact long-term prognosis.

Furthermore the findings from study 5 of the association between altered emotion expressivity and a range of clinical symptoms and social difficulties, could suggest that individuals with poor emotion expression represent a particularly challenging subgroup to treat. This group of patients may find it particularly difficult to engage

in standard psychological treatment and may require treatment to be tailored to meet their complex psychological and social needs. These findings also highlight the need for treatments to acknowledge not only difficulties with emotion expression, but also the particular difficulties with the expression of positive emotions (Tchanturia et al., 2015). The potential differences in the social cognitive profiles of children and adolescents and adults with AN should also be considered, and treatments should be tailored to suit different developmental stages, as well as different stages of severity.

Taken as a whole, the findings from studies 4 and 5 provide support for the development and implementation of treatments seeking to directly target these underlying mechanisms in both children and adolescents and adults, and also offer insights into specific mechanisms that may be beneficial targets for treatments and that could lead to substantial improvements in both functional and psychosocial functioning.

8.5 STUDY STRENGTHS

A general strength across this series of studies is the clinical applicability of its findings. Effective treatments for AN are lacking and the empirical findings from the experimental studies in this thesis hold translational value in regards to developing new treatments.

The strengths of each individual study will now be summarised.

Study 1: This is one of the largest studies of set shifting and central coherence in the child and adolescent AN field. A further strength is its use of robust neuropsychological tasks that were chosen in accordance with prior reviews of the existing child and adolescent studies as well as the most popular tasks used within the adult AN literature. In addition, this study also reported the same outcomes as many of the adult AN studies. The combination of these factors meant that the results of the current study were comparable with the existing literature. This study ensured that there were no significant differences in age between the AN and HC groups, and therefore both groups should have been at similar developmental stages. The inclusion of an analysis to test for the possible effects of psychopharmacological treatments on neuropsychological processing was a further strength of this study. In addition, whereas many other neuropsychological studies in adults and adolescents with AN have employed a short measure of IQ (such as the National Adult Reading Scale, (NART (Nelson & Willison, 1991)), this study employed the Wechsler Abbreviated Scale of Intelligence (WASI), allowing for a calculation of verbal and performance IQ as well as a full scale IQ.

Study 2: This study employed robust and widely used neuropsychological tasks.

Study 3: Study 3 was the first study in the field to assess the feasibility and acceptability of CRT in a self-help format. Furthermore, it also incorporated carers as a core part of the treatment. This study also collected both qualitative and quantitative methods. Data collected via qualitative interviews is likely to be rich in quality and may capture information that quantitative data might otherwise miss. The data gathered from this study will serve to improve self-help manuals and the delivery of CRT further.

Study 4: This is the first study to employ this body motion paradigm with children and adolescents with AN. A further strength lies in the inclusion of both adults and children and adolescents, allowing for the assessment of the effect of age/stage.

Study 5: This is the largest study in the field of eating disorders to investigate emotion expression. It also included a wide age range with the inclusion of both adult and children and adolescents. Furthermore, the administration of battery of self-report measures allowed for the assessment of numerous clinical correlates of altered emotion expression in young people.

8.6 STUDY LIMITATIONS

8.6.1 Measures

8.6.1.1 Neuropsychological measures

Although the neuropsychological measures employed in this study are validated and commonly used across the ED and wider psychiatric field, the limitations of the use of such tests require acknowledgement.

Both the WCST and ROCFT are complex cognitive measures. These measures have therefore been criticised as they do not solely measure one property and can tap into multiple functions. The WCST output contains scores measuring various abilities; however, importantly, it is possible to separate out general errors and responses from perseverative ones. Similarly the way in which the ROCFT is administered and scored can capture different abilities. Historically, the delayed recall of the ROCFT used a measure of global processing. However, this method is now generally considered to be a proxy measure of holistic processing that is vulnerable to contamination by other functions (such as memory), and there is research from the autism literature suggesting that the scoring method adopted in the current study is the most direct and 'pure' measure of global processing (Booth, 2006).

It is therefore recommended that future studies report both raw and percentage perseverative errors from the WCST and score the ROCFT according to Booth's (2006) method. Consistencies in reporting and scoring will allow for comparisons across studies to be made.

Central coherence is measured across a continuum from detail focussed processing to holistic and global processing. The measures employed by this study (the ROCFT and the FPT) are measures where performance is benefited by taking a global approach. The interpretations of this study are limited as it did not include a measure of central coherence upon which performance is benefited from a detail focussed approach, such as the Group Embedded Figures Test, meaning it was not

possible to assess for Weak Central Coherence (WCC; poor global processing with a bias toward details). Future studies should incorporate a measure of detailed-focussed processing to allow for the assessment of WCC in children and adolescents with AN.

8.6.1.2 Self-report measures

The self-report measures employed in these studies were established with validity and reliability, and allowed for the reporting of the subjective experiences of participants that may have not been recorded otherwise. However, a limitation of self-report measures lies in the fact that they are vulnerable to biases such as reporter bias.

8.6.2 Measurement of weight/ weight loss

Percentage ideal body weight was used as a measure of weight status for children and adolescents in this study, with an inclusion criteria for the AN group across studies 1, 4 and 5 of a %IBW of 90 or below. Child guidelines suggest that this fulfils an underweight criterion (Centers for Disease Control & Prevention). A limitation of using this method as a measure of weight is that premorbid weight and degree of weight loss was not accounted for. It is likely that premorbid weight will vary greatly between participants and thus, so will the current state of starvation for each individual at the time of testing. It was not possible to account for premorbid weight in the analysis of the current studies' results, and future studies should record this data.

8.6.3 Inclusion criteria

At the start of the study the inclusion criteria for HC participants with regard to weight was having a BMI within the healthy range (BMI=26 or under). However, this criterion was negatively impacting on recruitment, particularly within the

recruitment for study 2. Therefore, the inclusion criteria for HCs in regard to weight was relaxed and individuals were able to participate if their BMI was 30 or under.

8.6.4 Study design

The studies presented in this thesis were of a cross-sectional design, and therefore the observations made are limited to a single point in time. Although the data from these studies does add evidence to suggest there may be trait characteristics, long-term follow up data would be required to make firm conclusions. Furthermore, the effects of genetic and environmental factors on neuropsychological processing cannot be separated in these studies, and although the findings from study 2 suggest a genetic component, the influence of shared environmental factors in families cannot be ruled out.

8.6.5 Diagnosis

This psychiatric group of this study only included individuals with a current diagnosis of AN or AN-EDNOS. However, it is very common for individuals with EDs to regularly migrate between the different ED diagnosis categories and there is large heterogeneity in symptoms between individuals. Sub-types of AN were not recorded in this study (restriction or binge/purge), and therefore it was not possible to analyse the data according to these groupings.

8.6.6 Power/sample size

The sample size for a majority of the studies in this thesis was adequate for detecting statistical significance. However, within study 1 there was a trend toward group differences on the FPT. Group differences on this task have been observed within the adult population, and this may suggest that with a larger sample size, significant differences may have been observed within this study.

8.6.7 Participants

The child and adolescent participants in this study were mainly recruited from a day programme (an intensive treatment program) or from an outpatient service of a specialist child and adolescent national service. Although the severity of patients varies across this service, it could be argued that the sample is restricted by severity (a national service may have a higher referral of treatment refractory cases), and may not be totally representative of all AN populations.

Furthermore, although patients within these services had a current diagnosis of AN, they were at different stages of treatment at the time of testing, and this could have impacted on the results of the study.

This study only included females with a diagnosis of AN, and since there is emerging evidence that males with EDs may be characterised by a slightly different neuropsychological profile, the findings are not generalisable to males with ED. It is important for future studies to be inclusive of males with EDs.

8.6.8 Recruitment bias

Although the psychiatric group of this study was recruited through consecutive referrals to clinical eating disorder services, not all patients accepted participation in the study. This raises the question of whether there may have been a selection bias with differences between individuals that chose to participate and those who declined.

8.7 FUTURE DIRECTIONS

8.7.1 Long-term follow up data

Whilst the results of these studies in combination with preliminary genetic studies, add support to the notion that inefficient cognitive processing may be an endophenotypic trait in AN, it is acknowledged that the design of this study limits any direct inference. Without longitudinal data demonstrating the persistence of such characteristics following recovery and full weight restoration, we cannot say with certainty that they are truly traits and independent of the illness. Furthermore, we cannot elucidate the extent to which such characteristics may also be the result of neuroadaptation to the starved state in individuals with severe and enduring AN (Treasure et al., 2014). Future studies should therefore aim to collect such longitudinal data for both neuropsychological and socio-emotional processing in both children and adolescents and adults.

8.7.2 Neurobiological correlates of neuropsychological and socio-emotional processing in children and adolescents with AN

There is data from structural neuroimaging studies to suggest differences in brain structure in AN in both adults and children, such as enlargement of cortical sulci indicating brain atrophy (Eynde et al., 2012; Kerem & Katzman, 2003). The structural differences in brain volume have been associated with the clinical characteristics of AN, such as low BMI. Greater levels of atrophy have been related to more clinically severe cases (Boghi et al., 2011; Fonville, Giampietro, Williams, Simmons, & Tchanturia, 2014c), whilst other studies have linked lower brain volumes with the ability to maintain low weight (Zhu & Wang, 2008). Imaging studies with recovered patients have suggested that brain volume can improve with weight-restoration (Favaro et al., 2012; McCormick et al., 2008).

Taken together these studies suggest that whilst these structural changes in the brain could increase the treatment-resistance of AN, they are likely to be a consequence of starvation.

Additionally, atrophy to specific brain regions has been associated with impairments in ability or function of that area in adults with AN. There have been two studies assessing this in children and adolescents with AN, demonstrating opposing findings. Castro-Fornieles et al. (2009) found that greater reduction to the temporal and parietal regions of those with AN was correlated with lower levels of holistic processing on the ROCFT, suggesting that these structural differences may contribute to the cognitive processing style observed in children and adolescents with AN. However, Chui et al. (2008) failed to find any association between inefficient cognitive processing and structural abnormalities in 66 adolescents with AN.

The conflicting findings of these studies suggest that it may be beneficial to pursue this avenue of research using robust neuropsychological measures such as the WCST. Combining structural and neuropsychological testing across age groups in AN could also assist with controlling for possible brain maturational differences between children and adolescents and adults.

Functional magnetic imagining (fMRI) has been used to attempt to elucidate the neural underpinnings of inefficient cognitive and socio-emotional processing in AN. Studies of adults with AN have demonstrated differential patterns of brain activation between AN and HCs during the performance of cognitive or socio-emotional tasks. Whilst Fonville et al. (2013) found no differences in behavioural performance on the group embedded figures test between AN and HCs, fMRI revealed that individuals with AN used more neural effort to perform the task. Similarly Lao-Kaim et al. (2015) demonstrated aberrant brain activity in AN participants whilst switching set on the WCST, which suggested higher levels of neuronal effort was required by individuals with AN to perform the task to a similar standard as the HC group. Fonville et al. (2014b) also found increased blood-oxygen-level dependent (BOLD) signal in the fusiform gyrus during the recognition of positive facial emotions, also suggesting a higher level of neural effort was required by the AN group to perform to the same levels as the HCs.

Interestingly a small pilot study exploring the effects of CRT on task related brain activation found that after 10 sessions of CRT AN patients processed information in a more efficient manner, reflected by reduced neuronal activation post treatment.

Post-treatment, this activation was almost comparable to HCs (Fonville et al., 2014a).

To our knowledge, there are no studies using fMRI to investigate cognitive and socio-emotional processing in younger AN populations. This data could offer valuable insights into the neuroprogressive status of AN, for example, whether such neurobiological changes are associated with cognitive profiles at different stages of illness, both in terms of chronicity and severity. This data could also be coupled with treatment outcomes, to possibly shed light on different illness trajectories and predictors of treatment response.

8.7.3 Examination of neuropsychological and socio-emotional processing across eating disorder diagnoses

There is evidence from the adult ED literature of different cognitive processing profiles across the different diagnoses (AN, BN, BED, and obesity, (Wu et al., 2014)). However, there is currently a lack of studies investigating cognitive and socio-emotional processing in the EDs other than AN in children and adolescents. This data could provide information with regard to different aetiological risk factors of different EDs and subsequently provide specific treatment targets for each disorder.

8.7.4 Replication of pilot studies

Following the results of studies 2 and 3 (particularly the latter), it would be beneficial for future studies to replicate these findings with larger sample sizes.
Furthermore, in addition to the replication of study 3, it would also be beneficial to conduct a randomised control trial (RCT) of self-help CRT with carers with the inclusion of a comparison or control treatment. The addition of a health economic analysis of self-help CRT would also be desirable.

8.8 OVERALL CONCLUSION

In conclusion, the findings from this thesis provide valuable data aiding our understanding of aetiological and maintaining factors in AN. The results of study 1 demonstrated the presence of inefficient cognitive processing in children and adolescents with AN, and study 2 provided some evidence of the genetic underpinnings of these characteristics. The results of studies 4 and 5 added to the existing literature implicating socio-emotional processing difficulties as predisposing and maintaining factors, as well as producing novel experimental evidence of these abilities in children and adolescents with AN. When taken in context with the findings from the adult AN literature they provide valuable insights into differential cognitive and socio-emotional profiles that are possibly related to different stages of illness within AN, and an interaction between illness related factors and typical developmental trajectories.

These findings hold important translational value for the treatment of AN, and support the notion for the development and implementation of treatments directly targeting these underlying features. Data from this study has provided a research base to suggest that CRT would be beneficial for young people with AN, as well as data suggesting that the inclusion of family members could also prove beneficial. Additionally, pilot data was also provided to support the idea of self-help CRT within a family context. These studies have also highlighted the importance of treatments placing specific emphasis on areas of emotion processing that could serve to maintain AN and trigger a more severe and enduring prognosis.

CHAPTER 9

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CHAPTER 10

APPENDICES